Prevention, Policies and Priorities to Reduce the Impact of Malaria on US Military Forces

August 2011
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14. ABSTRACT

Malaria remains a significant force health pro-tection issue and Service members contracting malaria continue to make headlines in the national news. The Medical Surveillance Monthly Report describes the greatest number of P. falciparum cases in the Department of Defense (DoD) since 2003 and malaria consistently ranks as the most important infectious disease threat to the U.S. military.1,2 Although progress has been noted in some areas (e.g. decline in P. vivax and malaria cases in Korea), malaria exposures in Afghanistan and Africa continue to put Service members at risk. Despite known strategies to prevent malaria, protective measures and prevention practices are not uniformly implemented in the DoD. In August 2011, the Armed Forces Health Surveil-lance Center (AFHSC) hosted the 2011 DoD Malaria Stakeholder Meeting in Silver Spring, Maryland. Entitled ?Prevention, Policies and Priorities to Reduce the Impact of Malaria on U.S. Military Forces?, this DoD Malaria Stakeholder meeting was co-sponsored with the Office of the Secretary of Defense/Health Affairs (OSD/HA Force Health Protection & Readiness) and the Joint Preventive Medicine Policy Group (JPMPG). Dr. George Taylor (Deputy, ASD FHP&R) welcomed the more than 50 participants from across the Armed Forces and charged them to find Tri-Service solutions to reduce the malaria burden in our DoD troops. With representation from the operational, public health, preventive medicine, infectious disease, ento-mology, pest management, training, and research communities, participating DoD organizations included OSD/HA; U.S. Combatant Commands (AFRICOM, CENTCOM, SOUTHCOM, PACOM, SOCOM); Armed Forces Pest Management Board (AFPMB); National Center for Medical Intelligence (NCMI); Walter Reed Army Institute of Research; Navy Medical Personnel, Training and Education Command; and the research & development, public health, and headquarters commands of the U.S. Army, Air Force, Navy, and Marine Corps.

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EXECUTIVE SUMMARY

Prevention, Policies and Priorities to Reduce the Impact of Malaria on U.S. Military Forces

DoD Malaria Stakeholder Meeting

24-25 August 2011

Malaria remains a significant force health protection issue and Service members contracting malaria continue to make headlines in the national news. The Medical Surveillance Monthly Report describes the greatest number of *P. falciparum* cases in the Department of Defense (DoD) since 2003 and malaria consistently ranks as the most important infectious disease threat to the U.S. military.[1,2] Although progress has been noted in some areas (e.g. decline in *P. vivax* and malaria cases in Korea), malaria exposures in Afghanistan and Africa continue to put Service members at risk. Despite known strategies to prevent malaria, protective measures and prevention practices are not uniformly implemented in the DoD.

In August 2011, the Armed Forces Health Surveillance Center (AFHSC) hosted the 2011 DoD Malaria Stakeholder Meeting in Silver Spring, Maryland. Entitled "**Prevention, Policies and Priorities to Reduce the Impact of Malaria on U.S. Military Forces**", this DoD Malaria Stakeholder meeting was co-sponsored with the Office of the Secretary of Defense/Health Affairs (OSD/HA Force Health Protection & Readiness) and the Joint Preventive Medicine Policy Group (JPMPG). Dr. George Taylor (Deputy, ASD FHP&R) welcomed the more than 50 participants from across the Armed Forces and charged them to find Tri-Service solutions to reduce the malaria burden in our DoD troops. With representation from the operational, public health, preventive medicine, infectious disease, entomology, pest management, training, and research communities, participating DoD organizations included OSD/HA; U.S. Combatant Commands (AFRICOM, CENTCOM, SOUTHCOM, PACOM, SOCOM); Armed Forces Pest Management Board (AFPMB); National Center for Medical Intelligence (NCMI); Walter Reed Army Institute of Research; Navy Medical Personnel, Training and Education Command; and the research & development, public health, and headquarters commands of the U.S. Army, Air Force, Navy, and Marine Corps.

This year's DoD Malaria Stakeholder meeting was built upon the success and progress made from last year's 2010 Inter-Agency Malaria Meeting that engaged subject matter experts from the DoD, Centers for Disease Control and Prevention, Department of State, Department of Homeland Security, and the Peace Corps. Significant discussions addressed the need to improve diagnostic testing, clinical algorithms, and medical provider training, and how these activities directly affect data quality, malaria surveillance, military readiness and patient care. Additionally, attendees identified the lack of compliance with malaria chemoprophylaxis and protective equipment— preventive measures known to be effective— as significant issues that warranted further discussion. Considerable dialogue had surrounded chemoprophylaxis options and policy, and the need for standardized malaria policy, education and training of DoD medical personnel including guidance on malaria diagnosis, prophylaxis and treatment.

The 1.5-day Malaria Stakeholder meeting included didactic lectures and expert panels from DoD and foreign military subject matter experts, followed by frank open discussions. To address the many issues identified during the 2010 Inter-Agency meeting, this meeting's objectives were to:

- Provide an update regarding data and information sharing practices and continue to address gaps in surveillance, prevention and treatment programs;
- Address policy issues regarding malaria chemoprophylaxis;
- Delineate malaria-specific requirements and strategies for COCOM support; and
- Begin collaborations for development of clinical decision support tools and laboratory diagnostic support.

Setting the stage for this venue was an account of the preventive medicine experience from Oper-

ation Unified Response. In the aftermath of the Haiti earthquake, deployed personnel failed to take malaria chemoprophylaxis as prescribed, arrived with limited supplies and protective equipment, often didn't take the necessary precautions for vector control or avoidance, and had poor comprehension of the disease threat. This poignant vignette highlighted the persistent need for leadership oversight and accountability, and the challenges in ensuring compliance with personal protective measures— including chemoprophylaxis regimens.

This stakeholder forum addressed topics particularly relevant to DoD to include: COCOM requirements and priorities, malaria chemoprophylaxis, malaria diagnostics and microscopy, malaria resources and knowledge management, personal protective measures compliance, pest management developments, and military-military engagements. Breakout sessions were leveraged to maximize productivity and to ensure actionable strategies and specific deliverables. Breakout sessions focused on:

1) **Malaria Chemoprophylaxis**: A draft policy was presented for review and discussion which proposed: Malarone® as the drug of choice for high-transmission settings; Malarone® or doxycycline as drugs of choice for low-transmission settings; Malarone® as the preferred chemoprophylaxis agent for short-term deployments; directly observed therapy in high-risk environments; and NCMI as the resource to determine risk categories. Tremendous discussion was generated, and although there were differing opinions, the majority of individuals agreed with the policy's tenets.
2) **Malaria Microscopy and Training**: Standardizing malaria diagnostic slidesets and support materials for incorporation into the training curriculum was deemed to be of substantial benefit to medical techs/corpstaff, junior physicians, infectious disease specialists, and foreign partners.
3) **Personal Protective Measures (PPM) Compliance**: Troop PPM non-compliance was attributed to the lack of risk appreciation. The lack of perceived threat and leadership by line commanders was identified as major obstacles to enforcing PPM policies and practices.
4) **Malaria Resources and Knowledge Management**: Consensus was reached that Services should share existing malaria resources, collaborate to create new resources and coordinate to archive resources in a common location. Participants agreed that training materials were needed for troops, line leadership, deployed medical personnel, and all echelons of healthcare providers— with the designated priority being a malaria clinical practice guideline and diagnostic algorithm.

As a direct result of this 2011 Malaria Stakeholder meeting, AFRICOM immediately enacted a new chemoprophylaxis policy; a draft Health Affairs policy for malaria chemoprophylaxis was vetted to JPMPG for deliberation; overseas laboratories agreed to work with training and education commands to improve malaria microscopy slide sets and training; the Armed Forces Infectious Disease Society agreed to create a malaria clinical practice guideline and diagnostic algorithm; and the Armed Forces Pest Management Board is pursuing better educational materials and products to improve compliance with personal protective measures along with integrating PPM fundamentals into senior leadership curricula. Stakeholders also determined that future efforts should include the inventory and archival of DoD malaria resources in a common location.

NEXT STEPS: All of the respondents completing a post-meeting evaluation considered the symposium a valuable forum and very relevant to DoD force health protection issues. Attendees were enthusiastic about the progress made at this meeting; strategies were outlined for each of the topics, with stakeholders agreeing to continue working independently to capitalize upon the momentum generated. Issues identified for future discussion include improving the availability and validity of rapid diagnostic tests (with AFRICOM as the primary proponent) and addressing the ambiguities associated with primaquine policy and use.

ACKNOWLEDGEMENTS: AFHSC would like to thank the symposium speakers and participants for their presentations and engaging discussions. Special appreciation is extended to Ms. Priya Baliga and Ms. Jennifer Cockrill for their invaluable administrative and epidemiologic support of this forum. The opinions expressed herein are the views of the authors and do not reflect the official position of the Department of Defense or any of its organizations.

[1] AFHSC. *Update: Malaria, US Armed Forces 2010.* MSMR 2011; 18(1):2-6.

[2] Burnette et al. *Infectious diseases investment decision evaluation algorithm: a quantitative algorithm for prioritization of naturally occurring infectious disease threats to the U.S. military.* Mil Med 2008; 173(2):174-81.

Proceedings of the 2011 DoD Malaria Stakeholder Meeting

1. Introduction

The workshop commenced with **"Introductory Remarks"** by CAPT Kevin Russell (Director, Armed Forces Health Surveillance Center (AFHSC)) who provided an overview of the AFHSC's current worldwide Department of Defense (DoD) malaria efforts, which are funded in the amount of $9.9 million and engaged with 24 different partners around the globe. Additionally, he outlined the desired outcomes of the meeting:

1) A DoD chemoprophylaxis policy recommendation to Health Affairs;
2) An executive summary for all participants;
3) Endorsement of the Global Emerging Infections Surveillance and Response System (GEIS) partners' microscopy training project to improve the diagnosis of malaria in deployed environments; and
4) A plan for the future: subcommittees created for special topics and which outlines the next steps associated with those projects.

Following CAPT Russell's opening remarks, Dr. George P. Taylor (Deputy Assistant Secretary for Force Health Protection and Readiness) gave the **"Welcoming Address"**, focusing on DoD's challenges regarding malaria. He charged the attendees to find Tri-Service solutions to reduce the burden of malaria in our DoD troops. With force health protection as the priority, the economic factor is of secondary importance if treatment costs and mission compromise can be averted. Dr. Taylor emphasized the desire for the standardization of malaria policies across Services regarding prevention and treatment; and was interested in understanding if there was truly a necessity for Service-specific differences. He wanted to ensure that any existing discrepancies are due to operational differences between Services, such as organizational construct or the way a Service deploys forces, rather than simply differences in opinions. Due to the frequency of joint operations, policies that differ by Service make implementation of these disparate policies by the Combatant Commands (COCOMs) very difficult. An additional challenge addressed by Dr. Taylor was the malaria research budget. Dr. Taylor stressed that sustaining a reasonable amount of money in the malaria research budget will be a future challenge; therefore, priorities need to be identified with regards to prevention and treatment of malaria in order to optimally use the funds provided.

COL Mark Fukuda and CDR Annette Von Thun (AFHSC) provided a recap and "**Update of the 2010 Inter-Agency Malaria Symposium"** which engaged subject matter experts from the DoD, Centers for Disease Control and Prevention (CDC), Department of State, Department of Homeland Security, the President's Malaria Initiative and the Peace Corps. The 2010 meeting focused on malaria surveillance, data sharing, reporting systems, and communications. Surveillance gaps and other issues were identified and discussed. Significant deliberations addressed the need to improve diagnostic testing, clinical algorithms, and medical provider training, and how these activities directly affect data quality and malaria surveillance. Additionally, attendees identified the lack of compliance with malaria chemoprophylaxis and protective equipment— preventive measures known to be effective— as significant issues that warranted further discussion.

Several partnerships and products were developed as a result of last year's meeting. The AFHSC entered into an agreement via a memorandum of understanding with the CDC to address concerns about data quality, the perceived lack of reporting by the DoD, and the possibility of DoD malaria cases being seen in the civilian care setting. This data sharing agreement provides for the bidirectional data transfer of reported malaria cases to address these concerns. Through this case analysis, AFHSC was able to determine that 86% of data provided by the CDC is already captured by the DoD. In order to improve medical event reporting and to assist the Service hubs in identifying additional malaria cases, AFHSC created a monthly malaria case-finding report using the various data sources that it has available (inpatient records, outpatient visits, reportable events, theater encounters, and medical evacuations). Feedback from the Services has been favorable as it has allowed them greater visibility of actual and suspected malaria cases. The Medical Surveillance Monthly Report (MSMR), an AFHSC publication that features a malaria issue every January, leveraged an expanded malaria case definition as a result of last year's meeting.[1] The Epidemiology & Analysis division at the AFHSC continues to explore other case definitions to further improve capture of malaria cases, including leveraging HL7 laboratory data. However efforts to create COCOM-based reports have been challenged by issues with identifying cohorts at risk by either unit identification codes or personnel deployment records.

To set the stage for the 2011 DoD Stakeholder forum, LCDR Natalie Wells (Navy Bureau of Medicine and Surgery, (BUMED)), discussed "**Malaria and the Haiti Deployment Experience**". As the head of the Forward Deployed Preventive Medicine Unit assigned to Haiti following the earthquake in 2010, she shared her experience and challenges in addressing the diagnosis and prevention of malaria in DoD personnel. Opportunities to improve adherence to force health protection (FHP) recommendations were identified. All deployed personnel were given chemoprophylaxis prior to deployment. However, due to the rapid nature of the deployment, many troops did not have adequate supplies for malaria prevention such as DEET, bed nets, and permethrin to treat uniforms. Eleven individuals were identified during this deployment as having malaria: 91% used doxycycline for chemoprophylaxis, 78% reported missing doses, the average time to symptom onset was 30 days (range 10-42 days), and there was a 3-day delay (average) in presenting for care. As part of the malaria outbreak investigation, LCDR Wells and her team found that assigned personnel at the identified camp, had permethrin-treated uniforms, but over a third of the 109 Service members reported missing at least two consecutive doses of doxycycline chemoprophylaxis during the preceding two weeks and reported only sporadic use of DEET. In comparing two adjacent camps with similar environmental conditions, the differences in malaria case rates were attributed to differences in command leadership and troop compliance with chemoprophylaxis (directly observed therapy vs. personal responsibility). The team found many reasons for non-adherence with chemoprophylaxis including the lack of a perceived malaria threat, disruption of daily routines, and perception of medication ineffectiveness.[2] Interventions included administering Malarone® to the entire unit, accountability for taking chemoprophylaxis, indoor residual spraying of tents, vector control and abatement, and compliance with DEET application. Opportunities identified

[1] Armed Forces Health Surveillance Center. Update: Malaria, U.S. Armed Forces, 2010. *Medical Surveillance Monthly Report (MSMR).* 2011; Vol 18(1): 2-6.

[2] Mung K, Renamy B, Vely JF, Magloire R, et al. Malaria Acquired in Haiti 2010. *Morbidity and Mortality Weekly Report*. March 5, 2010; 59(8): 217-219.

from this deployment to prevent future outbreaks include: improvements in the communication of health threats, pre-deployment provisioning of personal protective equipment, longer-acting chemoprophylaxis medications, better training for medical department representatives, and greater personal and line leadership accountability.

2. Malaria Prevention – The COCOM Perspective

Representatives from each of the COCOMs in attendance participated in a panel discussion on "**Malaria Prevention: The COCOM Perspective—Perceived Needs and Challenges**". The panel consisted of CAPT Gail Hathaway (U.S. Pacific Command representative), COL Frederic Plotkin (U.S. Southern Command), LTC Jennifer Caci (U.S. Special Operations Command representative), MAJ Brad Gardiner (U.S. Central Command), and Maj Robert Holmes (U.S. Africa Command).

Maj Holmes indicated that the three main priorities associated with malaria for the U.S. Africa Command (USAFRICOM) were chemoprophylaxis policy, online education, and rapid diagnostic testing. There is a high prevalence of infectious diseases, including malaria, within USAFRICOM's area of responsibility (AOR). As a high-profile and potentially fatal disease, malaria garners much attention from leadership, as it is both a line and medical issue requiring additional collaboration. Continuing to rely on doxycycline as the drug of choice is problematic in this AOR. Doxycycline's poor tolerability and short half-life has repeatedly been demonstrated to put deployers at risk. Seeking more reliable medications and incorporating these recommendations into policy is imperative. USAFRICOM leadership places tremendous importance on providing appropriate education for troops deploying to Africa regarding the risks associated with malaria, FHP measures, and the importance of chemoprophylaxis compliance. However, there is no standardized process or on-line training to ensure that force health protection messages are conveyed effectively and consistently. Force health protection begins with education; as such, an online tool would be beneficial in providing necessary malaria training and education prior to deployment to Africa. Additionally, training needs to be developed and supported for medical staff deploying to areas in USAFRICOM's AOR. The malaria rapid diagnostic test (RDT) is USAFRICOM's preferred testing method given the lack of fixed medical facilities and paucity of microscopy assets throughout the majority of their AOR. However, the current malaria RDT used by the DoD is not ideal for an operational environment since it lacks temperature stability, positive controls, and sensitivity for non-immune individuals. In addition to a next generation RDT, clinical decision tools, diagnostic algorithms, and training should be developed to support its use.

Composed of 36 countries, U.S. Pacific Command (USPACOM) is the largest AOR by surface area and is primarily a maritime domain. The AOR will be subdivided in the near future with the Marine Corps assuming responsibility for Southeast Asia, the Army assuming responsibility for South Asia, the Navy assuming maritime responsibility and the Air Force assisting as needed. There is a fairly high incidence of malaria in the USPACOM area—with most DoD cases attributed to Korea. USPACOM is headquartered in Hawaii, has robust laboratories that conduct malaria research in Thailand (Armed Forces Research Institute for Medical Sciences (AFRIMS)) and Cambodia (Navy Medical Research Unit (NAMRU-2)), and maintains strong relationships with the CDC and the World Health Organization (WHO). CAPT Hathaway indicated one of PACOM's primary concerns is obtaining better data to

determine the prevalent infectious diseases in an area prior to deployment. Reliable and timely data for risk assessments are necessary to recommend appropriate force health protection measures to protect our Service members.

The U.S. Central Command (USCENTCOM) defined their priorities as: 1) consistent, simple, delegable guidance regarding chemoprophylaxis use policy; 2) better, more accurate malaria risk assessment stratification for the AOR to minimize differences associated with different sources (e.g. National Center for Medical Intelligence (NCMI), WHO, and CDC websites); and 3) user-friendly personal protective equipment (PPE) that troops can easily use and obtain. To that end, MAJ Gardiner relayed that USCENTCOM has established a malaria working group to develop a policy regarding the use of malaria prophylaxis in Afghanistan. The working group is recommending a seasonal approach (Apr-Nov) as opposed to year-round usage of chemoprophylaxis, in an effort to increase compliance. The draft USCENTCOM policy (MOD 11) is otherwise reportedly similar to the draft "Policy Memorandum on Medications for Prophylaxis of Malaria" (Appendix A). Logistical issues were acknowledged if chemoprophylaxis medications were administered on a seasonal basis, particularly amongst those personnel deployed for longer periods spanning on and off seasons, who may be introduced to a new chemoprophylactic agent during their deployment, or for those that are considered frequent deployers.

Both vivax and falciparum malaria are endemic to the U.S. Southern Command (USSOUTHCOM) region. USSOUTHCOM has put forth their own guidance regarding chemoprophylaxis for travel within their AOR, but COL Plotkin stated that his command would be willing to modify USSOUTHCOM policy to support a more efficacious medication. COL Plotkin agreed with the need to pursue next generation RDTs with the accompanying clinical practice guidelines and diagnostic algorithms. Additionally, he concurred with the need to improve force health protection training, especially in the use of PPE and chemoprophylaxis, for those deploying to malarious areas.

The U.S. Special Operations Command (USSOCOM) representative, LTC Caci, expressed concern for the real-world challenges of providing care to the war-fighter in the field. Having a policy that is well articulated, logically consistent throughout the region, and that advocated for the best (vice cheapest or easiest) chemoprophylaxis strategy to protect deployed personnel was one of the foremost priorities. The logistics of medication delivery and acquisition has been historically problematic. Obtaining sufficient quantities of medications has been a recurring issue. For example, the U.S. Army Medical Command is supposed to provide all chemoprophylaxis medications prior to deployment for Army personnel, but often the Service member is directed to obtain additional needed medications in country. Access to atovaquone/proquanil (Malarone®) has also been a challenge because, as a more expensive alternative, military treatment facility (MTF) pharmacies are unwilling to budget for or provide the medication. Additionally, obtaining bednets has been logistically problematic. Finally, addressing the need for greater diagnostic support—either well-performing rapid diagnostic tests, the ability to have reach back support, or well-trained local microscopy resources—would be advantageous to providing care in austere environments.

3. Malaria Chemoprophylaxis Policy

Lt Col Bruno Pradines (Institut de Recherche Biomédicale des Armées) and Prof Jacques Le Bras (Institut de Médecine et d'Epidémiologie Appliquée) began the chemoprophylaxis session of the curriculum with their presentations collectively entitled "**Malaria Chemoprophylaxis & Force Health Protection – the French Experience**". The French have a long history of malaria efforts within Africa including research and capacity building engagements in Niger, Senegal, Côte D'Ivoire, Gabon, Mali, Cameroon, Democratic Republic of the Congo and Djibouti. Studies in Senegal have demonstrated that malaria is becoming progressively more resistant to mefloquine and artemisinin. Lt Col Pradines discussed the use of doxycycline in the French Army, which was first used as chemoprophylaxis due to increasing mefloquine resistance. The main problems noted with the use of doxycycline in the French Army included non-compliance, medication intolerance, and an elimination half-life of 16 hours which does not permit significant therapeutic margin if inconsistently taken. Additional studies have discerned that there is an increase in doxycycline resistance (as measured by increasing IC_{50}) associated with genetic polymorphisms and an increase in copy numbers of molecular markers that convey resistance—providing further concern about relying upon doxycycline as the primary chemoprophylactic agent in this area.

Professor La Bras conveyed that most cases of malaria in France are directly attributed to travelers; eighty percent of which were *P. falciparum*. When examining the reason for failures in French malaria patients, independent of the medication prescribed, the sheer majority of malaria cases were either attributed to no chemoprophylaxis or were associated with false declarations of correct chemoprophylaxis (per suboptimal drug levels measured in blood). Professor La Bras discussed the use of Malarone® as prophylaxis in France and described low failure rates and rare occurrences of resistance. In a case study of approximately 350 patients, very few cases were associated with true failures—6 failures were attributed to doxycycline, 3 cases were attributed to mefloquine failure, and no failures were noted with Malarone®. In fact, worldwide use of Malarone® for last year (2010) was examined with only one identified prophylaxis failure and 20 cases of true treatment failures, despite 1.2 million-weeks of prophylaxis and nearly 10,000 treatment regimens.

CDR Greg Deye (Walter Reed Army Institute for Research (WRAIR)) presented the major premises of the "**DoD Proposed Malaria Chemoprophylaxis Policy and Rationale**". As one of the stakeholders instrumental in drafting the proposed policy (Appendix A), CDR Deye explained that the policy was created to address the concerns that the existing policies are outdated, fragmented and do not adequately address the role of Malarone®. Because there is no guidance for its use, some MTF pharmacies are not making Malarone® available since cheaper alternatives exist. Thus a multi-disciplinary group of subject matter experts drafted the proposed policy for review and discussion by meeting participants, with the intent of updating the ASD(HA) October 2002 memorandum, "Anti-Malarial Medications".

CDR Deye addressed the rationale for using risk stratification to provide different recommendations for high-transmission (Malarone® as drug of choice) and low-transmission (Doxycycline or Malarone® as first line agents) settings. Risk stratification was selected based upon cost/benefit analyses which indicate that the costs associated with administering chemoprophylaxis are

high compared to the benefits the drugs may provide, particularly in low-transmission areas. The draft policy also provided guidance on the use of Malarone® for short-duration travel, directly observed therapy in austere high-risk environments, and leveraging NCMI as the resource to assess risk of malaria transmission (expressed as the rate of troop cases per month in the absence of protective measures).

The effectiveness of both doxycycline and Malarone® in high transmission areas, defined as places where malaria transmission rates range from 11-50%, were discussed. Because of its short half-life, it was emphasized that missing doses of doxycycline leads to a risk of prophylaxis failure. Tail dosing for doxycycline was noted to be 28 days, in contrast to the 7 days required for Malarone®. CDR Deye also conveyed that doxycycline has never been studied in individuals weighing greater than 70 kilograms—an issue of particular relevance to our American population. Medication tolerability is an additional concern with doxycycline. Doxycycline has been associated with photosensitivity and vaginitis, with adverse gastrointestinal side effects reported in 17-45% of individuals taking doxycycline hyclate,[3] the generic formulation currently used by the DoD. Doxycycline monohydrate is a formulation that has reduced gastrointestinal side effects and an improved safety record as compared to doxycycline hyclate, but it has an identical half-life and mechanism of action, is relatively more expensive ($1/pill vs. $.05/pill) and is not as readily available in MTF pharmacies. Malarone® was noted to be significantly more expensive ($3.83/pill), but has a considerably better tolerance profile, greater therapeutic margin, and relatively strong evidence which demonstrates that occasional skipped doses do not contribute to chemoprophylaxis failure (see Appendix B for comparison of doxycycline versus Malarone®). Successful use of Malarone® in the deployed setting has been demonstrated in a Swedish military study of 161 soldiers (approximately 800 person-months) who were prescribed Malarone® and none developed malaria.[4] To address concerns about inducing resistance in populations prophylaxed with Malarone®, CDR Deye stated such resistance is caused by treatment of semi-immune individuals and not the use of Malarone® or other prophylaxis drugs.[5]

Ms. Jennifer Cockrill (AFHSC) presented a case study of "**The Cost Implications of Malaria Prophylaxis Failure in U.S. Troops in a Malaria-Endemic Region of Africa"**. The study included 42 Service members who spent 19 days participating in a military exercise in a malaria-endemic area of Africa. Doxycycline or mefloquine were provided as chemoprophylaxis regimens prior to deployment. Six of these Service members contracted malaria with resultant hospitalizations upon their return to the U.S. Using figures from a previous study on the financial impact of a malaria outbreak on U.S. troops in Liberia[6], Ms. Cockrill estimated total treatment costs for these six Service members. Direct costs associated with clinical care, radiology exams, laboratory studies, medications, procedures,

[3] Tan KR, Magill AJ, Parise ME, Arquin PM. Doxycycline for malaria chemoprophylaxis and treatment: report from the CDC expert meeting on malaria chemoprophylaxis. *Am J Trop Med Hyg*. 2011; 84(4): 517-31.

[4] Andersson H, Askling HH, Falck B, Rombo L. Well-Tolerated Chemoprophylaxis Uniformly Prevented Swedish Soldiers from *Plasmodium falciparum* Malaria in Liberia, 2004-2006. *Military Medicine*. 2008; 173(12): 1194-1198.

[5] McKenzie FE, Jeffery GM, Collins WE. Gametocytemia and fever in human malaria infections. *J Parisitol.* 2007; 93(3): 627-33.

[6] Roberts A, Tamminga C, Wurapa E, Epstein J, Malone P, Hickey P, Whitman T, Richie T. Financial Impact of Malaria on U.S. Forces- 2003 Outbreak among Marines in Liberia. Poster presented at the 2011 Armed Forces Public Health Conference.

consultations, and other fees were estimated to be $105,000. Indirect costs attributed to lost duty pay for these individuals were estimated at almost $54,000. Cost calculations were conservative and did not include costs associated with transportation (medevacs), outpatient follow up visits, or additional base-pay associated with dependents. Further caveats included that lost duty time is an estimate and that outpatient malaria cases may not have been captured in the study—thus underestimating the true expenditures associated with this malaria outbreak.

Costs associated with the use of various chemoprophylaxis medications were factored into the analysis. Doxycycline hyclate and doxycycline monohydrate were the cheaper options with Malarone® serving as a relatively more costly alternative; costs for prophylaxis options ranged from $103 to $4500 total depending upon the medication. These expenses paled in comparison to the avoidable costs associated with treatment and lost duty time of the 6 malaria-infected Service members (estimated at $158,691). Thus, using this example of a relatively small contingent (42 personnel), for a relatively short duration deployment (<3 weeks), without any medevacs or mortality, and with a modest attack rate of 14.3% — the concern about the additional expense associated with using Malarone® chemoprophylaxis is not justifiable if it could have prevented even one case of malaria.

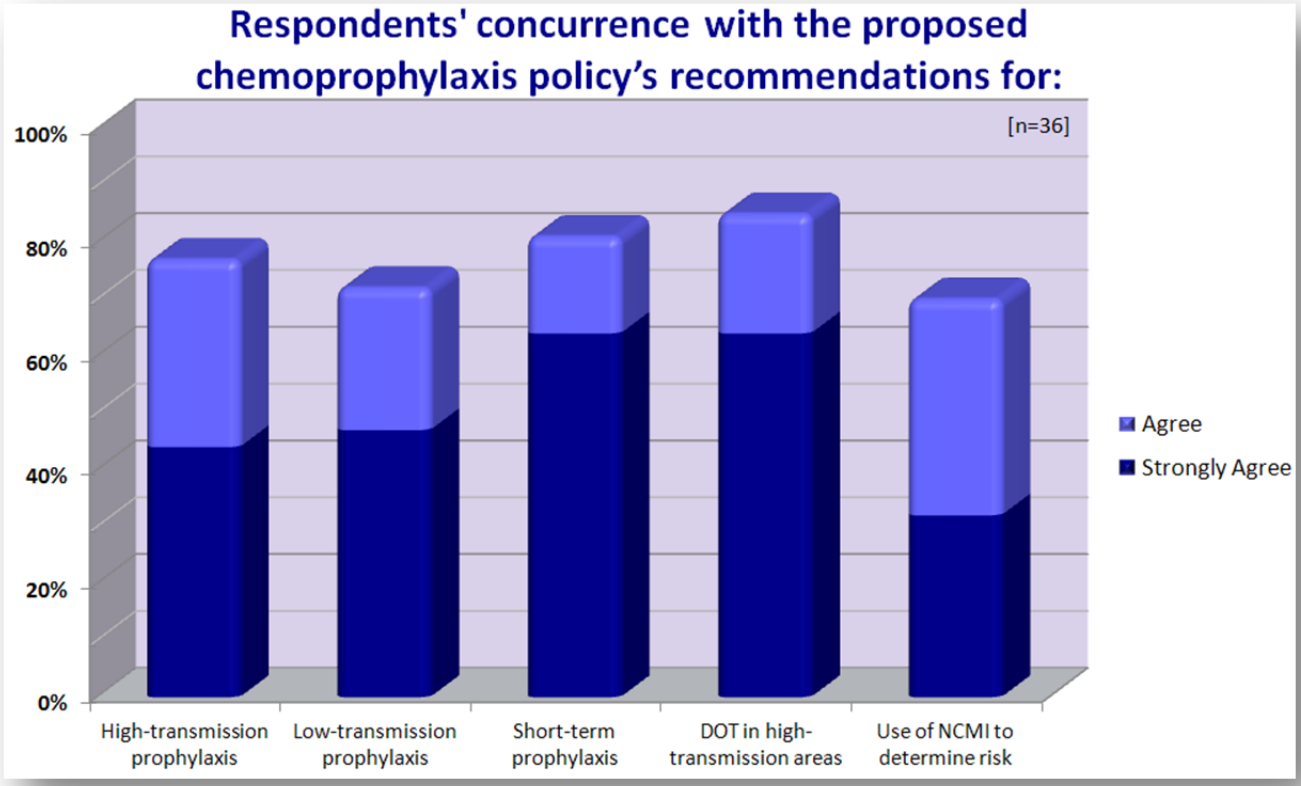
After the various presentations, COL Scott Stanek (OSD/Health Affairs (FHP&R)), opened the floor for a facilitated discussion regarding the **"Draft Malaria Chemoprophylaxis Policy Memorandum"**. It was stated that the military should take all necessary precautions to avoid any further malaria deaths (and cases), and that while the costs associated with prophylaxis may be perceived as high, it is important to emphasize that treatment costs would be diminished as a result of using a more robust and better tolerated chemoprophylaxis regimen. One participant noted that as long as Malarone® costs more, it will not be used as the priority medication. The caveat should be made that the cost of Malarone® is expected to decrease within the next one to three years when it loses its patent/proprietary rights. GlaxoSmithKline (GSK) has indicated that they may be willing to negotiate the unit price of Malarone® if the military were to select it as their primary malaria prophylaxis medication. One advantage to using a higher cost medication such as Malarone® is that it is less likely to be used for treatment in malaria-endemic countries, and thus has less risk of developing resistance.

Concerns were voiced about endorsing the use of NCMI as the sole risk assessment tool because of issues with obtaining quality information of sufficient granularity, timeliness and seasonal assessments. Preference was expressed in consulting other open risk assessment sources (e.g. CDC, WHO). Discussion then shifted to whether a new policy is truly needed to address malaria chemoprophylaxis, or whether it was the execution of the policy that was the real problem at hand. Some participants questioned the assumption that there are significant issues with doxycycline effectiveness and tolerability as a chemoprophylaxis agent to warrant a policy change. Other attendees expressed concern that the forum may be "medicalizing" a problem that is really a line commander issue. One participant noted that directly observed therapy (DOT) has been show to be effective regardless of which medication is used. However, pre-deployment and post-deployment periods are extremely challenging to ensure DOT compliance. Although there is a desire for head-to-head efficacy comparisons of Malarone® and doxycycline in real-world settings to justify the additional expense, true superiority studies do not currently exist, would be challenging to execute given the large study

populations required, and would be very hard to conduct in the military population and environment. However, one might assume that the improved tolerance (and resultant compliance), broader mechanism of action, and the longer half-life would result in greater effectiveness of Malarone®.

After the initial discussions on the first day, participants were surveyed as to how they would rank the various medications used for malaria chemoprophylaxis (doxycycline, mefloquine, or Malarone®). For high transmission settings, 84% of respondents indicated that Malarone® would be their drug of choice. For low transmission settings, the participants were split between Malarone® (51%) and doxycycline (48%) as their first choice. Additionally, participants were queried as to their concurrence with the five main tenets of the draft policy (Figure 1). DOT was the recommendation which received the most robust support by attendees. In contrast, utilization of NCMI as the means of determining high and low risk transmission status garnered the least amount of support.

Figure 1.



At the end of the second day of deliberations, meeting participants were able to come to the following conclusions: 1) Most participants agreed that a new malaria chemoprophylaxis policy is necessary and should supersede existing policies rather than supplementing current guidance. 2) Consensus was reached in recommending DOT in high-risk settings. 3) Most accepted Malarone® as the drug of choice in high-risk areas, although there seemed to be some dissention based upon Service and specialty affiliation. 4) A revised policy should provide flexibility to allow for difference in regions, shipboard duty, deployment settings (urban environment vs. austere conditions), etc. 5) The new policy

should not address malaria treatment or rapid diagnostic tests. 6) Guidance regarding the use of primaquine for terminal prophylaxis requires further discussion and clarification. 7) Concern was expressed about using NCMI as the sole resource for risk determination. 8) Some Navy representatives expressed concern about the complete exclusion of mefloquine as a viable chemoprophylactic agent for appropriate patient populations. 9) Consensus verbiage for the high-risk guidance (paragraph 4a) was created to modify the draft chemoprophylaxis policy (Appendix C).

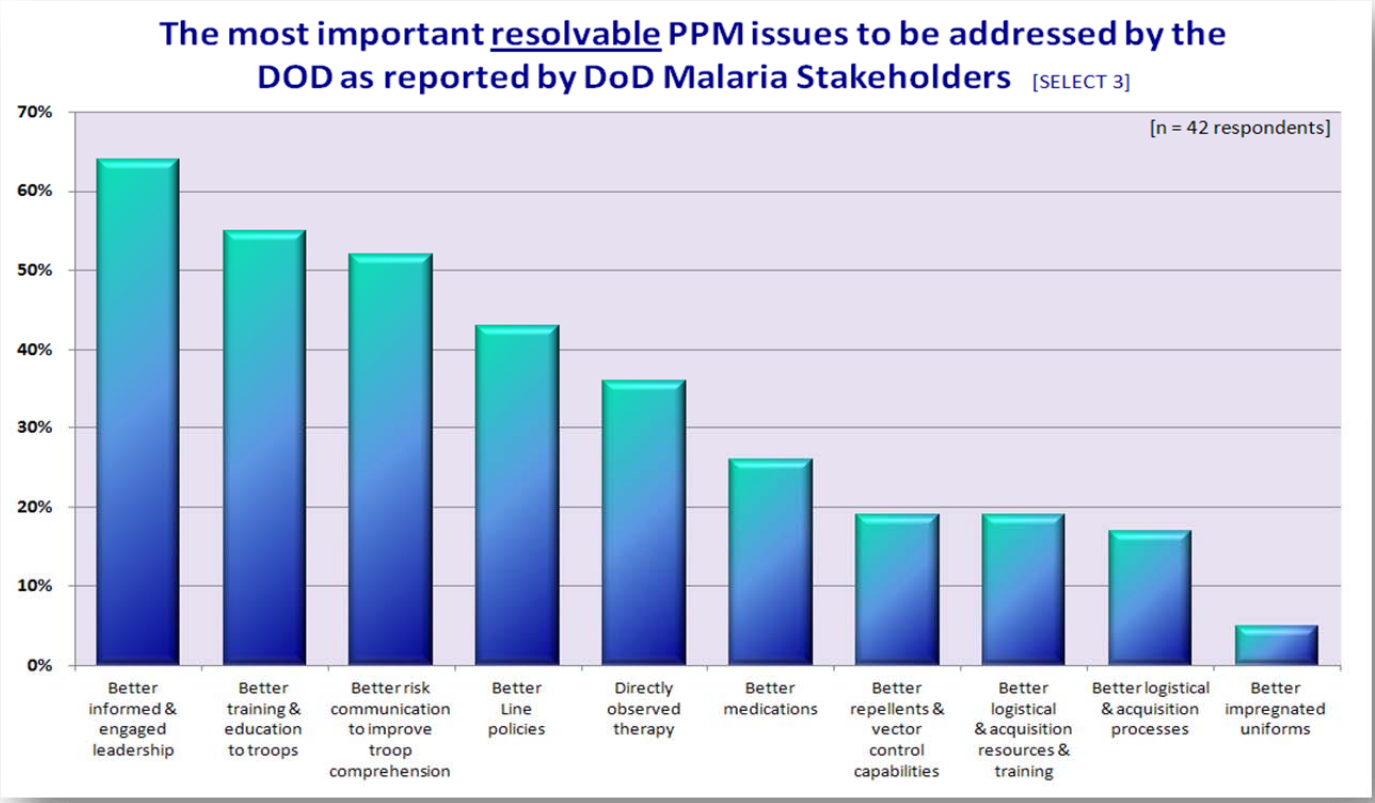
NEXT STEPS: AFHSC will formally present the draft proposal to the Joint Preventive Medicine Policy Group for their action and further discussion. Once deliberated, revised and staffed, it will be forwarded to Health Affairs (FHP&R) for their action and approval after ratification by the Force Health Protection Integration Council. It is recommended that a new policy should completely replace (vice supplement) all previous malaria chemoprophylaxis policies—but that it should not address malaria treatment or rapid diagnostic tests. The consensus verbiage for the high-risk guidance created by the stakeholders will be forwarded, concerns about using NCMI as the risk resource will be relayed, and the issues expressed by stakeholders in this forum will be conveyed. Guidance regarding primaquine use for terminal prophylaxis remains an outstanding (and relevant) item for discussion.

4. Personal Protective Measures (PPM) Compliance

CDR Steven Rankin (Armed Forces Pest Management Board (AFPMB)) gave a presentation **"AFPMB: A Unique Global Asset"** which highlighted the Deployed Warfighter Protection (DWFP) Program. The mission of the AFPMB is to "ensure that U.S. Forces have the most effective vector control and pest management capabilities to prevent adverse effects on troops, weapons systems, supplies, equipment, and installations and to ensure maximal risk reduction through the use of best pest management and environmental practices". Areas of emphasis of the DWFP program include novel insecticide chemistries and formulations, personal protective systems, and application technologies targeting mosquitoes, phlebotomines, other flies and general vectors. Accomplishments of the program include numerous collaborations, publications, patents and inventions. CDR Rankin also elaborated upon many of the innovative and ongoing projects to include development of permethrin treatment for new uniforms, alternative spatial mosquito repellents, and other novel vector control mechanisms that have promising applications for providing protection against malaria and other vector-caused diseases.

Survey questions addressing PPM practices and opinions were administered the symposium to serve as topics for further discussion. Respondents felt that the most significant barriers in complying with PPM were attributed to a lack of emphasis and/or comprehension by leadership (71%); lack of risk appreciation by troops (62%); logistical or acquisition constraints, limitations and challenges (40%); lack of comprehension by troops (38%); and unintentional medication noncompliance (38%). PPM interventions deemed to have the most impact in reducing the risk of malaria included: chemoprophylaxis (76%), repellents (43%), bednets (38%), pesticides & vector control (29%), impregnated uniforms (17%), after hours clothing/repellants (17%), and proper uniform wear (14%). Those PPM noncompliance issues deemed to be the most resolvable by DoD stakeholders are presented in Figure 2.

Figure 2.



Significant discussion addressed the need for greater line leadership. The lack of leadership and perceived threat by line commanders was identified as among the major obstacles in enforcing PPM policies and practices. The line needs more directive policy from medical (e.g., directly observed therapy) and those policies must be highlighted in DoD and Service documents, and not just promulgated by the individual Services' Surgeon General. To address this knowledge gap, participants

argued for the incorporation of PPM principles into the myriad of Joint- and Service- specific senior and mid-level leadership (officer and enlisted) course curricula.

Training and risk communication continues to be a major issue for ensuring consistent line leadership support and field compliance across all levels. Noncompliance with known PPM strategies by deployed personnel, although multi-factorial, is predominantly ascribed to a lack of risk appreciation, lack of comprehension, and human nature. The behavior of personnel (e.g. sleeping outside of bed nets due to warm climate, exercising and relaxing outside of permethrin-treated uniforms, etc.) often prohibit PPM effectiveness. New countermeasures to potentially circumvent these behaviors include spatial repellents that could be used in tents and novel repellent cuffs or bands that only need to be worn around the arms and/or legs.

Improving training and risk communication could be accomplished by using innovative strategies to reach a younger, more technologically savvy audience to reinforce the basic principles of malaria prevention and control. Current DoD and Service resources need to be evaluated for gaps and refined with new tools identified for development. Potential new approaches could include pre-deployment on-line training, digital phone reminders and applications, video clips (AFN spots and infomercials), social networking sites, video games, and providing more audience-appropriate "messaging" to connect with the enlisted troops. Making the training or applications more relevant and reflective of real world scenarios might emphasize the importance of PPM compliance to the deployed Service members.

When queried about how to specifically improve PPM compliance based on "Lessons Learned", the following suggestions were offered along the themes of improving risk communication,

Cdr David Wilcox (Health Services Attaché, Canadian Defence Liaison Staff) gave a presentation entitled, **"Malaria and Canadian Forces Health Services"** during which he conveyed results from a recent survey* assessing the use of personal protective measures (PPM) in Canadian Forces deployed to Afghanistan.

Self-reported PPM use:

- 11% applied DEET
- 21% used bednets
- 78% wore insecticide treated clothing
- Only 4% used all 3 PPM

- Persons perceiving risk of exposure as high were more likely to use bed nets and repellent; perceived seriousness of disease was not significantly associated with reported use of any intervention.
- Individuals reminded to use an intervention had higher odds of doing so.
- Officers and senior non-commissioned members reported greater PPM use than junior non-commissioned members.
- Personnel spending more than 4 hours outside at night (on a daily basis) during the preceding two weeks had significantly lower odds of using bednets.
- Persons spending more than 24 hours outside the main camp in the preceding month had significantly lower odds of using bednets, but higher odds of using repellent.
- Respondents using one PPM were more likely to use another.
- Odds of repellent use were more than twice as high for those who did not indicate a safety concern compared to those who did.
- Two-thirds of respondents used some other DEET than that issued (Ultrathon); however, persons using issued product were more likely to use it.

*Schofield S, Crane F, TepperM. Good Interventions that Few Use: Uptake of Insect Bite Precautions in a Group of Canadian Forces Personnel Deployed to Kabul, Afghanistan. *Military Medicine.* 2012; 177(2): 209-215.

re-tailoring education and training, and providing data-driven feedback to leadership.

- *"Improve education/training so that individuals and leaders know there are reasons and impact for a given policy; they are more likely to be compliant even if they can't remember why—they at least remember there was/is a good reason."*
- *"Educate troops that malaria chemoprophylaxis protects against almost NOTHING else (doxycycline covers spirochetes), whereas PPM will protect them against all other vector-borne threats."*
- *"Senior enlisted ownership of education is pivotal, specifically with regard to ineffective preventions, (e.g. skin-so-soft, matches, etc.). Just in time training for units as soon as first case occurs and involving line leadership, not just the medical department, is important."*
- *"Incorporate specific examples of morbidity and mortality (Liberia Sea Bee, Haiti) into troop education and leadership training."*
- *"Develop and use reminders on some periodic basis during a deployment or exercise—a strategy proven to be effective."*
- *"Incorporate questions on PPM compliance into the Post-Deployment Health Assessment to permit data analysis."*
- *"Develop and improve the collection of malaria information from any unit employing malaria PPM: feedback from chemoprophylaxis tolerance, DEET use/after action, vector control employed or not, etc."*
- *"Specific, defined method of communicating lessons learned to line leadership (e.g., # of cases, adherence to PPM) for buy-in and better education of troops."*

These types of interventions require significant DoD research, understanding of noncompliance variables, and advocacy for development, training, and educational assets to be directed towards identifying compliance failures, discovering innovative methodologies to minimize those failures, and developing or enhancing existing tools to better protect deployed forces.

NEXT STEPS: Because the mission of the AFPMB encompasses all of the issues brought forward, a separate committee was not considered necessary to further address these issues. The AFPMB will tackle the identified problems of 1) senior leadership training (e.g., incorporation of preventive medicine and pest management principles into War/Staff College curriculum); 2) troop training materials (specifically, risk communication and PPM compliance); and 3) advocacy for novel pest management methodologies; during their ongoing meetings. AFPMB will report their progress on these projects at future DoD Malaria Stakeholder Meetings.

5. Malaria Diagnostics and Training

MAJ Jacob Johnson (U.S. Army Medical Research Unit – Kenya (USAMRU-K)) provided the group with an update titled, **"GEIS Malaria Surveillance Steering Committee: Diagnostics"** on a proposed malaria microscopy training program. In order to assist COCOMs in force health protection efforts and to capitalize upon the expertise of the GEIS laboratory partners, the GEIS Malaria Surveillance Steering Committee (MSSC) proposed leveraging their microscopy expertise and pairing it with training

opportunities to improve microscopy proficiency of deployed medical personnel, DoD technical staff, and host nation partners.

Microscopy is currently the "gold standard" for malaria diagnosis and a primary endpoint in clinical trials. It allows for morphologic identification of species and the determination of parasite densities. Microscopy is critical for the accurate diagnosis of malaria which is pivotal to surveillance, research and clinical treatment. Additionally, microscopy is currently mandated to confirm all negative results obtained with the BinaxNOW® malaria rapid diagnostic test (per U.S. Food and Drug Administration (FDA) labeling) to ensure cases of malaria are not missed. Since 2004, the Malaria Diagnostics Center (MDC) at USAMRU-K has taught 50 microscopy courses and trained 937 laboratory technicians in malaria diagnostics. This training has included personnel from 25 African countries, the U.S., Ireland and Thailand. The MDC has established 3 malaria microscopy training centers in Ghana, Nigeria and Tanzania to support host nation capacity building efforts in these regions.

MAJ Johnson presented the MSSC's multifaceted malaria diagnostic program which encompasses training, quality assurance, and reference materials. In order to address the training needs of DoD medical staff and healthcare teams, their proposed initial step is to inventory and market the existing video, CD-ROM, and web-based microscopy training resources. Secondly, the GEIS partners propose supporting and supplementing existing training aimed at corpsmen/medical technicians, physicians, and deploying medical staff. He presented outlines for a one to two week "basic" microscopy course with both didactic and practical instruction in various malaria topics including (but not limited to): standard operating procedure development, laboratory quality assurance and quality control, parasite detection, *Plasmodium* species identification, and parasite counting. He also stressed the importance of pre- and post-tests, consisting of a written exam, slide reading, and species identification to document proficiency and measure improvement.

To train DoD technical staff, MAJ Johnson advised cross-training between DoD labs, creating a DoD certification program (more rigorous than the WHO certification program), and introducing a "train the trainer" program for DoD personnel to encourage host nation collaboration. He stressed the importance of training host nation partners and supporting capacity building to assist the COCOMs. To maintain quality systems, monitoring procedures through site visits, supportive supervision, and external quality assurance programs (including exchanging slides and providing feedback) is essential. Reference materials necessary for a good training program include national policies and guidelines, standard operating procedures, wall charts, and blood films which display the multitude of *Plasmodium* species, parasite stages and parasite densities.

As part of their unified effort, GEIS partners from across the DoD will collaborate to create a durable, high-quality, standardized, and uniformly prepared slide repository of malaria blood films (consisting of true-negative, individual *Plasmodium* species, mixed species (coinfection), low and high parasitemia slides) used for microscopy training, competency and proficiency assessments and other related quality assurance programs. This set of malaria diagnostic slides could then be incorporated into various training programs with different proficiency requirements based upon the needs of the trainee (e.g., medic/corpstaff, general medical officer (GMO), infectious disease specialist, laboratory

technician, researcher, professional microscopist). This blood collection program would also strive to establish a malaria blood sample repository for development and evaluation of emerging malaria diagnostics. MAJ Johnson outlined an approach for malaria blood collection, starting with a partnership between the DoD laboratories, standardization of critical procedures, collection of parasitized and non-parasitized whole blood samples, expansion of sample collection efforts, characterization of blood samples by expert microscopists and molecular assays, creation of blood film and whole blood sample repositories, and finally film set distribution. The anticipated outcome of these efforts will be 1) greater microscopy proficiency with resultant reduction in treatment delays and diagnostic errors; and 2) greater diagnostic capability and capacity by DoD personnel and host nation partners; thereby ultimately benefiting the COCOMs and our deployed forces.

MAJ Stuart D. Tyner (recently from AFRIMS) addressed **"Malaria Diagnostics Training"** and discussed malaria diagnostics, current training and DoD malaria diagnostic resources. He began his presentation by discussing the three primary diagnostic capabilities currently available within the DoD for malaria.

The malaria RDT allows point of care testing, with rapid results and ease of use. Minimal training is required, there are no cold chain requirements, and the compact, self-contained packaging has all the reagents included in the box. BinaxNOW® is currently the only FDA-approved product (although many others are manufactured outside the United States) and is available in boxes of 12 or 25 tests. However, a negative test result is not diagnostic. The malaria RDT is known to lack clinical sensitivity in non-immune populations (e.g., U.S. Forces); as such, negative results are not considered definitive. RDTs are often misread, and have the potential for false positives from persistent antigenemia from previous infections.

Another diagnostic modality used by the DoD is microscopy. Peripheral blood is obtained from finger sticks with thick and thin blood smears prepared with glass slides and Giemsa stain. Although microscopy has very high sensitivity (detecting only 5-10 parasites per microliter of blood), enables the calculation of parasitemia densities, and can define the *Plasmodium* species, it is dependent upon specific resources and technical proficiency. Necessary supplies, including electrical power, equipment, and solutions or clean water for reconstituting reagents, may not be available while deployed or when in resource-limited areas. Microscopy also requires initial proficiency training, and because it is a perishable technical skill set, it is reliant upon refresher or sustainment training.

Real-time polymerase chain reaction (PCR) is the most sensitive method for diagnosing malaria and is also able to provide species-specific results. However, PCR is not presently part of the standard diagnostic inventory. It requires home-brewed laboratory assays, and is not currently supported by the Joint Biological Agent Identification and Detection System (JBAIDS)– the platform that most operational units are equipped with to diagnose biological agents. PCR also requires supplies, electrical power, equipment and a cold chain. It is very time- and technically-intensive, requiring a fully-trained laboratory specialist.

MAJ Tyner discussed current medical training specifically for malaria diagnostics within the DoD, stressing that options were rather limited for most DoD personnel. The DoD Medical Education and Training Campus (METC), located at Joint Base San Antonio – Fort Sam Houston, provides training for enlisted medical specialties and incorporates malaria diagnostics for laboratorian training, but with minimal emphasis in the curriculum for general medical technicians and corpstaff. USAFRICOM has partnered with WRAIR to employ an infectious disease threats training program which addresses malaria including a small emphasis on microscopy for just-in-time training targeted at deploying medical assets. The Uniformed Services University of Health Sciences (USUHS) offers an annual tropical medicine course for physicians and scientists, which is primarily didactic and covers the topic of malaria in its curriculum. Finally, USUHS also supports AFHSC-funded rotations at NAMRU-6 (Peru), USAMRU-K and AFRIMS for medical students, residents and infectious disease fellows which often incorporate malaria training into their overseas experience (Appendix D).

The DoD research community, through its overseas labs, has a number of malaria diagnostic resources and assets. NAMRU-6 has experts in malaria diagnostics; USAMRU-K and AFRIMS have malaria diagnostics training programs with expert WHO-certified microscopists; and, although not a DoD-specific resource, the Australian Army Malaria Institute is a GEIS partner and USPACOM resource that has malaria diagnostics capabilities in Brisbane, Australia. Using the assets that the DoD already has available, MAJ Tyner put forth the proposal of a basic malaria diagnostics training program incorporated into the enlisted medical training curriculum (see Appendix E for METC Point Paper). Utilizing a train-the-trainer construct, METC instructors would participate in a five-day didactic and experiential training course taught by expert microscopists from USAMRU-K, AFRIMS, and NAMRU-6. The five-day course would focus on slide making, staining, and reading and will incorporate pre- and post-testing for quantifiable results, leveraging the MSSC slidesets. These instructors would also have a two-day refresher course at six-month intervals to ensure retention of information learned. The training would ideally be conducted at METC but could also take place at an overseas laboratory or at WRAIR.

During the ensuing facilitated discussion, **"Microscopy and Diagnostic Training Needs"** led by CDR David Brett-Major, the challenges of malaria diagnostics in the operational environment were highlighted. In the deployed setting, there is a misconception that if an RDT is available, the troops are well-equipped for malaria diagnosis. However, most infected non-immune individuals present when they have significant clinical symptoms but relatively low parasite density and hence, below the sensitivity threshold of the RDT. Unfortunately, clinicians are often tempted to delay intervention due to the lack of confirmatory results instead of considering the patient's condition—often times it is much easier to convince leadership that a response (e.g., medevac) is needed when there are definitive diagnostic test results. The stakeholders addressed these diagnostic needs in three main considerations—clinical goals, public health goals, and what is currently recognized as unknown regarding the use of microscopy.

Clinical Goals. The group asserted that if diagnostic testing is utilized in the field, it should be done on a rule-in rather than rule-out basis. The posture of a distributed medical asset should be towards empiric therapy for malaria in moderately or severely ill patients in the appropriate environmental setting. To be clinically useful, diagnostics should be rapid, quantitative or semi-

quantitative, and specific, leading to functional risk stratification of the patient. Participants believed that geographic setting, operational setting, team composition and resourcing would have significant impact on desirability and utilization of microscopy and other diagnostic modalities in the field. Participants acknowledged that in some instances, microscopy is a useful tool to motivate clinical providers to overcome barriers in administering therapy for malaria. Microscopy was also acknowledged as being useful in following patients and in helping to direct further therapy in the absence of a timely clinical response.

Public Health Goals. Clinical microscopy and other diagnostic modalities were recognized to assist the military health system beyond individual patient care. Case and outbreak identification, confirmation, and characterization of the parasite species, growth stage and burden are important contributors to a wide range of interventions including entomologic action, adjustment of unit and personal protective measures, screening for cases, and modifications to sustained or subsequent operational plans. These diagnostic modalities also promote command support for prevention and interventions through validation of threats. The stakeholders additionally recognized that some of these public health goals might be addressed by referral laboratory methods such as PCR testing of dried capillary blood blots.

Unknowns**.** Several unknown factors challenge the incorporation of microscopy and other diagnostic modalities into a comprehensive FHP strategy. Relative merit incorporating logistics, ease and accuracy of use and interpretation, and laboratory certification requirements complicate resolving microscopy versus rapid diagnostic testing in diagnostic algorithms. The current state of malaria microscopy training in the DoD is poor in contrast to global health program standards for entities which execute formal microscopic malarial diagnosis. While proposals exist to develop a cadre of experts, the likelihood of broad dissemination of such expertise throughout the force to make definitive malaria microscopy readily available is uncertain. Clinical and public health microscopy and other diagnostic algorithms may not be congruent for shared resources once optimized to their individual purposes. The operational performance of diagnostic testing in deployed populations on anti-malarial chemoprophylaxis has not been assessed.

The Way Ahead**.** Despite these challenges, participants felt that expertise in microscopy, rapid diagnostic testing and referral laboratory testing should be developed and pushed to the most distributed levels practicable. This expertise development should be consistent with parallel development of force health protection strategies. Deploying medical personnel should be familiar with malaria microscopy and rapid diagnostic testing to the level of useful interface with host nation resources or teleconsultation with DoD expertise. While a variety of robust clinical training options exist which incorporate this familiarization, they are not yet utilized sufficiently by those entering high risk areas of operation. A pipeline for sustainable malaria microscopy expertise does not yet exist for school houses, combat support hospitals, and tertiary care centers, although models are present throughout the DoD overseas laboratory network. A method for maintenance of proficiency and peer quality assurance, such as currently employed by the DoD overseas laboratory network, in support of existing and future malaria microscopy training and diagnostic centers, is needed.

When polled, 80% of participants thought that the MSSC microscopy training initiative would be valuable to the DoD and 70% agreed that it would be valuable to their designated community specifically. Surveyed participants specified the group that would benefit most from a malaria microscopy training initiative would be the enlisted technicians and corpsmen (58%), followed by general medical officers and junior physicians (32%); however, participants noted that all of the identified groups would significantly benefit from this initiative. Some participants felt that the proposed microscopy training program had little value in the deployed setting, where rapid test availability was seen as the major diagnostic asset. Others valued the training of host nation partners as an essential resource that could be called upon when deployed to remote areas.

Discussion during the breakout groups centered on current malaria RDTs and a second generation test. There was sentiment among the group that the point of care malaria diagnosis capability needs to be better, faster and cheaper than what the current test, BinaxNOW® offers. However, there are no known development efforts of a second generation test in progress. Other products are on the market outside the U.S. WHO has performed a product review, but these products are not FDA-approved. There needs to be a post-marketing survey of the BinaxNOW® RDT in order to have data-driven requirements to update, improve, and/or develop a new RDT. There is concern that the DoD research and development (R&D) community does not perceive the need for, nor have the money to dedicate toward, new malaria RDT efforts. Participants felt that the COCOM Surgeons had a pivotal role to play in pushing for new R&D in this field. The COCOM Surgeons, however, need subject matter consultants in order to become more informed on the topic.

A multi-faceted approach would be necessary to tackle the various issues associated with the current RDT and could potentially include: 1) Packaging of tests into smaller self-contained units—which could be addressed with the BinaxNOW® manufacturer (Alere), and would necessitate price re-negotiations. 2) Update of the package insert and pursuing the use of RDTs in the field independent of confirmatory microscopy testing—which would potentially require CLIA- and/or CLIP- waiver and would need to be addressed with the FDA via the U.S. Army Medical Research and Materiel Command (USAMRMC). 3) Consideration of other existing RDTs and determine (via clinical trials) whether there is a better performing product. 4) Pursuance of a second generation test by R&D that better meets the operational requirements of improved sensitivity (especially for *P. vivax)*, greater temperature-stability, and an incorporated positive control.

NEXT STEPS: MSSC and GEIS partners will proceed with the plan to create the comprehensive malaria diagnostic training slidesets and will distribute to officer and enlisted education and training commands when ready. Stakeholders at USUHS and METC acknowledged the relevance and need for these slidesets as diagnostic training aids and were committed to incorporating them into the existing training curriculum when they became available. As part of this plan, better marketing of existing training resources and courses would benefit the DoD in addressing this identified knowledge and skillset gap. Finally, pursuing the RDT agenda with USAFRICOM as the primary COCOM proponent—to include guidance on its use, efforts to address some of the post-marketing issues, and strategies to meet the short- and long-term operational requirements—will be needed to provide additional diagnostic support

to deployed medical assets. Dr. Magill (Defense Advanced Research Projects Agency) volunteered to generate the verbiage for the COCOMs to request assistance of MRMC in addressing the RDT issues.

6. Clinical Decision Support Tools and Knowledge Management

Representative from each Service (Army, Navy, and Air Force) were invited to provide an overview of **"Services' Malaria-Specific Resources and Gaps"**. Existing malaria-specific resources and clinical decision support tools for the diagnosis and treatment of malaria were highlighted. Perceived deficiencies were also shared which precipitated discussions on the gaps in malaria resources and knowledge management within the DoD.

LTC Laura Pacha (U.S. Army Public Health Command (USAPHC)) shared several malaria resources available through the U.S. Army (Appendix F). The Public Health Command has entomology posters and cards for risk communication; deployment health products including medical threat briefs and deployment health guides and cards; information on the DoD insect repellant system, deployment pest management resources and vector maps; and fact sheets on malaria risk communication, prevention and chemoprophylaxis.

LCDR Natalie Wells (BUMED) outlined Navy-specific resources in terms of policy and guidance, training, and organizations who serve as subject matter experts in the Navy. For policy and guidance, BUMED has a general malaria message (GENADMIN), 6th fleet message guidance, an "Interim Fleet Guidance for Deployments to Africa", and a comprehensive 106-page malaria pocket guide (Tech Manual) that discusses malaria biology, prevention, protective measures (to include chemoprophylaxis options), diagnosis, treatment, special circumstances and military malaria control and responsibilities. In terms of training, the Navy has a malaria laboratory identification course and an online malaria training course required for all deployers to the USAFRICOM AOR. Organizations involved in malaria support and resource management for the Navy include the Navy Entomology Center of Excellence, the Navy Environmental and Preventive Medicine Units, and the Navy and Marine Corps Public Health Center, which has a webpage devoted to malaria resources (Appendix F).

Maj Jessica Cowden (WRAIR) provided an overview of the Air Force's malaria resources, focusing predominantly on policy. She outlined several Air Force policies which addressed the topic of malaria chemoprophylaxis, treatment, and preventive measures. She delineated several points in need of clarification in the existing Air Force policies. For example, a conflict exists within the reporting instructions for USAF Africa regarding when chemoprophylaxis is required.

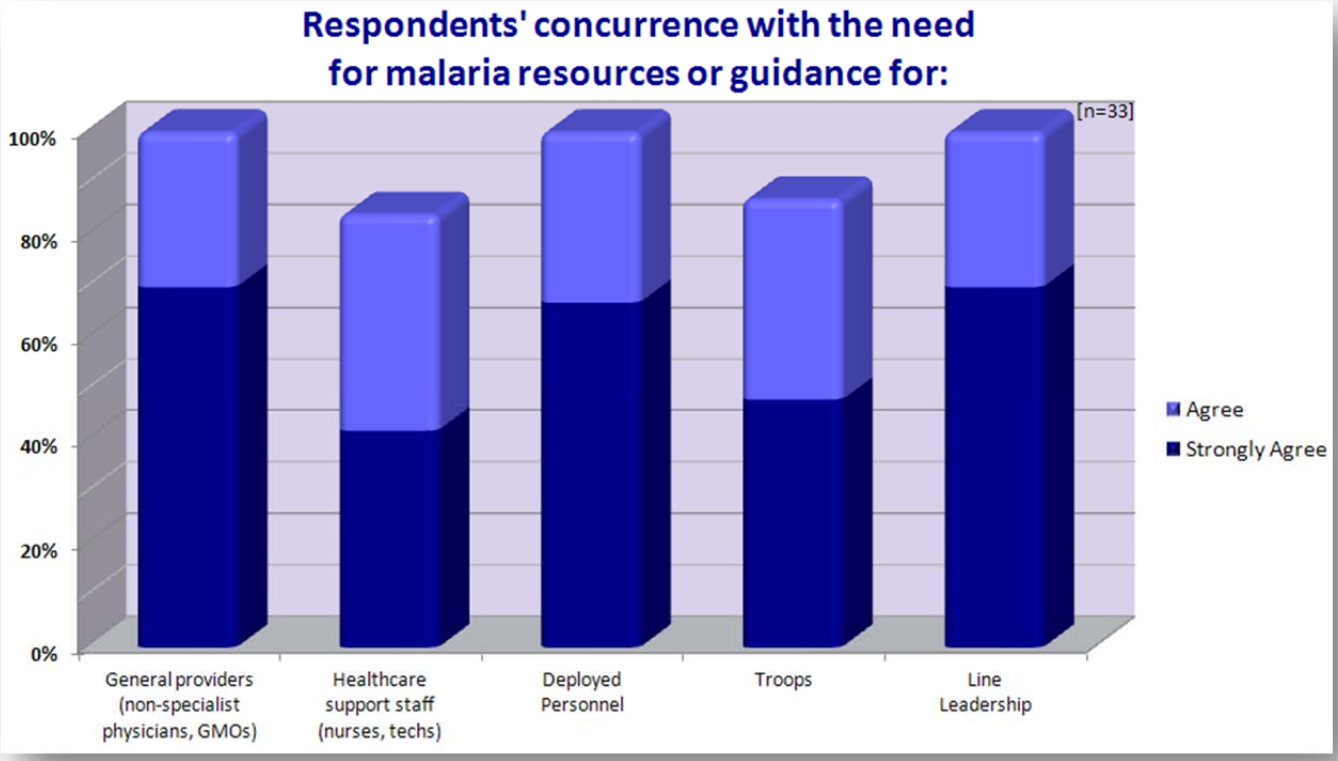
CDR Von Thun then facilitated the discussion addressing, **"Malaria Resources and the Need for Knowledge Management"**. In order to determine what other potential malaria resources were available, representatives from other Services and COCOMs were queried. The audience was not familiar with any unique Coast Guard resources. [*N.B.* USCG has a Malaria Prevention and Control instruction.] Representatives from the Marine Corps, were not aware of any headquarter or Marine Expeditionary Force (MEF) specific training, policies, or other resources. The Public Health Service leverages the tremendous assets available from the CDC and National Institutes of Health (NIH) for malaria prevention, diagnosis and treatment. Both USAFRICOM and USCENTCOM have specific policies

addressing malaria force health protection measures. With the exception of USAFRICOM, which is in the process of developing COCOM-specific training and resources, there were no additional assets conveyed by other COCOM representatives. It was noted that in addition to WRAIR- and USUHS-offered curricula, the Services host several types of tropical medicine and malarial microscopy and diagnostics training through their respective educational and training or public health commands (Appendix D).

Discussion next focused on perceived gaps and resource deficiencies. The lack of accessible training, especially for deploying personnel, and the lack of clinical decision support tools were the primary gaps identified. In fact, 91% of survey respondents agreed that there was a need for malaria diagnostic algorithms (to include the role of rapid diagnostic tests) and 75% of respondents declared a need for clinical practice guidelines for malaria treatment.

When queried as to which audiences have a need for development of additional malaria resources, conference participants unanimously identified general providers/physicians (e.g., non-specialists, GMOs), line leadership, and deployed personnel. However, greater than 80% of survey respondents also specified that troops and all echelons of heathcare providers require additional malaria resources and training materials (Figure 3).

Figure 3.



Knowledge management—defined as the management of information and training resources across the Armed Forces—was the next topic of conversation. Survey respondents expressed

concurrence with the statements that Services should share existing malaria resources (94%), collaborate to create new resources (88%), and coordinate to archive resources in a common location (88%), with over 90% of participants specifying that there was a need for malaria knowledge management in the DoD.

The group deliberated upon the pros and cons of having a centralized DoD repository for knowledge management of malaria resources. If centrally located, it would be much easier for the Services and troops to share resources, disseminate information, ensure consistency, and conserve efforts. Logistically, however, determining where the website would be hosted and who would be responsible for keeping the information updated would be a potential challenge and would need to be delineated. The Deployment Health Clinical Center (DHCC) website[7] was highlighted as a potential solution. As an existing, service-independent website, the DHCC webpage has already established a compendium of Service, DoD and non-DoD malaria resources.

Successful strategies proffered to enhance the adoption and utilization of existing guidance and resources include: 1) Single location (one-stop shopping) placed on an easily accessible website or other medium; 2) Extensive cross-posting/cross-linking with a robust marketing and education campaign; 3) Centrally-funded development of risk communication resources with the medical education and training commands inserting guidance into existing training pathways; 4) On-line training options to include COCOM requirements for pre-deployment education with the same tool for all Services. When polled where the archive should be located, 45% thought the Services should post to their own websites, 42% favored the existing malaria webpage on the DHCC website, and 39% specified the AFHSC website.

The breakout session participants further discussed details involved in knowledge management logistics and delineated some of the challenges that would need to be addressed. All agreed that consolidation and organization of resources needed to be in one central location (with links on specific Service sites). This proposed website would also need to provide force health protection and pre-deployment intel; policy and guidance; general information; available courses and web-based training (with certificates); and clinical resources to include diagnostic algorithms, clinical practice guidelines, and contact information for consultant "reach back" support. Additionally, the website must be accessible (not CAC-restricted or on a .mil site); all Services' materials must be represented (if centralized/combined); and different information will be needed for the various levels of healthcare personnel (providers, lab technicians, enlisted healthcare staff) as well as lay public, interested Service members, and family members. Recommendations included: forming a committee to manage the process; having this committee designate one Service to take the lead; having the committee comprised of infectious disease specialists, preventive medicine physicians and a representative from the Joint Chiefs of Staff (to share with NATO colleagues); products would be produced collaboratively with a critical review of the webpage occurring every 1-2 years to assess resources' currency and relevance.

[7] https://www.pdhealth.mil/malaria.asp

The breakout session also addressed the need for clinical decision support tools. Based on the collective sentiment that a CPG for the field would be most helpful, these stakeholders determined that the CPG should be evidence-based, symptom-driven (presented as evaluation of fever), and provide guidance on evaluation, diagnosis, and treatment. Items to be addressed in this CPG include the use of RDTs, guidance for presumptive treatment, criteria for medevac, specimen collection for confirmatory testing, and contact information for reach back support. This CPG would ideally have buy-in from the Infectious Diseases Society of America (IDSA) and/or the International Society of Travel Medicine (ISTM).

NEXT STEPS: AFHSC will request that the Armed Forces Infectious Diseases Society (AFIDS) establish a sub-committee to develop a CPG based on the evaluation of fever. The plan is to keep the AFID's working group small (5-10 people) and include infectious disease consultants, malaria experts, and preventive medicine representation. Once drafted, the CPG may need to be vetted for use in the field environment. In response to the need to further knowledge management efforts, a subcommittee should be formed to explore options and take the initial steps in coordinating the website location, organization and content. Part of this process would require an initial "map and gap"—an inventory of existing materials and an assessment of resources that may need to be created, refined, or developed (Appendix F). Initially, this subcommittee meeting might be hosted by AFHSC or one of the Services.

7. Malaria Treatment Options

COL Bryan Smith (U.S. Army Medical Materiel Development Activity (USAMMDA)) provided an update on **"Intravenous Artesunate: The New Generation of Lifesaving Treatment for Severe Malaria in the Warfighter"**. Beginning with a description of the Pharmaceutical Systems Project Management Office (PMSMO), COL Smith shared that the mission of PSPMO is to "manage DoD resources applied to the advanced development of pharmaceutical products (e.g., drugs, vaccines, biologicals, diagnostics, blood products) for use by the U.S. military". The PMSMO is tasked with moving products to U.S. licensure and fielding within the framework of DoD acquisition regulations and policies, and the consumer protection laws of the FDA and the U.S. Environmental Protection Agency. The mission is accomplished by establishing partnerships with industry (foreign and domestic), other governmental agencies (U.S. and outside the continental U.S. (OCONUS)), and academia. The PSPMO serves as an investor, broker, manager, and facilitator on behalf of the DoD and the U.S. Army Medical Research and Materiel Command (USAMRMC).

Although quinine is the currently approved medication for severe malaria in much of the world, resistance to quinine is increasing and has potentially significant toxicity. These side effects may include: cinchonism (tinnitus, blurred vision, headache); cardiac arrhythmias (QTc prolongation) with torsades de pointe; hypotension (associated with intravenous use); hypoglycemia with increased insulinemia; immune thrombocytopenic purpura; and "Blackwater fever" (hemolytic anemia, hemoglobinuria, and often acute renal failure).

Since 1991, quinidine gluconate has been the only parenteral (intravenous) formulation available in the United States. Current supplies are threatened— limiting the medication's availability for cardiology interventions. Rapid infusion of quinidine is also associated with peripheral vascular

collapse and hypotension. The side effect profile of quinidine is qualitatively similar to quinine— with cinchonism and hypotension— however the cardiac dysrhythmias precipitated by quinidine are more frequently observed and thus pose a greater risk.

The discovery and subsequent development of a new medication to treat severe and complicated malaria would be a great addition to the anti-malarial arsenal. Qing hao (wormwood) is the plant from which the medication artesunate is derived. Artesunate administered intravenously (IV) has been granted investigational new drug (IND) status as a provisional drug for the treatment of severe malaria. WRAIR has produced 11,000 vials of the medication for compassionate use which is administered by the CDC's Domestic Response Unit & Malaria Branch. IV artesunate is pre-positioned at CDC quarantine stations throughout the continental United States and Hawaii, with a similar configuration of distribution hubs throughout the Canadian Malaria Network. Requests for IV artesunate from the DoD for its warfighters are coordinated through the CDC, with stockpiles pre-positioned at the U.S. Army medical centers located in Germany and Korea. Once a patient is approved by the CDC as an appropriate candidate, the DoD then coordinates with the necessary organizations for medication delivery and IND protocol adherence. To date, artesunate has proven to be an effective and invaluable medication for providing rapid treatment to severe malarial cases. One hundred seventeen individuals with severe malaria have received artesunate, with no attributable deaths and no significant delays in medication administration (average time from request to treatment is 7 hours). New drug application (NDA) filing for IV artesunate is expected to occur in the next 18-24 months.

8. Malaria Prevention – Role of Militaries

Dr. Refaat Hanna (USAFRICOM), gave a brief presentation on "**Malaria-Related Military to Military Engagements within USAFRICOM**". Malaria is a particular problem for militaries because of its ability to cause sudden epidemics which can hinder or even halt military operations. Similar to deploying U.S. military forces, African soldiers face the risk of malaria infection when deploying to areas where they experience heavier malaria exposure or are exposed to strains different from those present in their country of origin. The impact of malaria on peacekeeping operations in Africa has been identified by the African Union as one of the major issues that affects their missions.[8] High malaria infection rates among African military personnel hamper their ability to participate in peacekeeping operations. Failure to protect troops against malaria can also impact the outcome of conflicts. Malaria causes more disabilities among peacekeeping forces than combat injuries—and, is the second most prevalent infectious diagnosis (after respiratory tract infections) as noted by routine surveillance during a recent AMISOM (African Union Mission in Somalia) deployment. Military treatment facilities, both in garrison and when deployed, are responsible for providing care to civilian beneficiaries, who represent the majority of patients seen with malaria.

[8] African Union. The Impact of HIV/AIDS, Tuberculosis and Malaria on the World of Work in Africa, October 2, 2009. Proceedings from the 7th Ordinary Session of the Labour and Social Affairs Commission of the African Union. Available at: http://www.africa-union.org/root/ar/index/LSC-EXP-10%20(VII)The%20Impact%20of%20HIV%20TB%20%20Malaria%20on%20the%20world%20of%20work%20in%20Africa%20(2).doc

During the recently hosted USAFRICOM Surgeon's Malaria Symposium in April 2011, African delegates put forth a proposal aimed at producing a long-term malaria prevention strategy for the militaries of sub-Saharan Africa. Delegates envisioned a task force that would identify components needed for an effective malaria prevention program, standards against which each nation may use to assess critical needs. These requirements may be matched with defense, non-defense and non-governmental agencies' programs for promoting the building of health system capabilities and capacity. A questionnaire was disseminated to solicit input on each country's existing military malaria activities, willingness to participate in a malaria task force, expected level of participation, and the perceived needs and outcomes of the proposed malaria task force. The findings of this questionnaire will result in the formation of a regional network of engaged militaries seeking to address the challenges of malaria prevention and control in a concerted manner with the assistance of USAFRICOM, and other U.S. agencies.

COL Colin Ohrt (WRAIR) lectured on the **"Role for Militaries in Malaria Mortality Reduction and Elimination"**. WRAIR—in their mission to discover and develop new pharmaceutical agents to reduce mortality, morbidity and impact global public health from parasitic diseases—has been the nation's primary developer of new drugs to prevent and/or treat malaria. Many of the anti-malarial medications that we have today are a result of WRAIR's development to include: chloroquine, primaquine, mefloquine, doxycycline, Malarone® and aretesunate. Today, there is a new era of emphasis on malaria control and elimination with examples including the 2015 Millennium Development Goals (sidebar), the involvement of the Bill and Melinda Gates Foundation, the call to chart a course for malaria eradication, and the creation of the U.S. Government's President's Malaria Initiative. There is a distinct lack of attention paid to malaria control efforts focused on foreign Ministries of Defense. This gap produces an ideal opportunity for military-military malaria control efforts that would benefit both the DoD and partner countries' military populations.

Millenium Development Goal 6: Combat HIV/AIDS, malaria, and other diseases

Target 6C: Have halted by 2015 and begun to reverse the incidence of malaria and other major diseases

- *Prevalence and death rates associated with malaria*
- *Proportion of children under 5 sleeping under insecticide-treated bednets*
- *Proportion of children under 5 with fever who are treated with appropriate anti-malarial drugs*

Reference:
http://www.un.org/millenniumgoals/aids.shtml

The way ahead to malaria reduction and eradication would involve a multi-faceted approach to address vector control, migrant populations (including troops), chemoprophylaxis and intermittent treatment therapies, access and adherence to treatment regimens, medication quality control, drug resistance, disease surveillance, and diagnostic capabilities. WRAIR has been instrumental in assisting other nations' militaries throughout a variety of interventions to include: artemisinin resistance containment and chemoprophylaxis trials (Cambodia); microscopy training and new diagnostics assessments (Kenya); surveillance, training and advisement of mitigation strategies for troop malaria dissemination (Indonesia); and real-time surveillance, provision of rapid diagnostic tests, diagnostic and treatment education programs, bed net distribution and monitoring, and training of village health workers (Tanzania).

9. Conclusions and Way Forward

There are many facets to the DoD malaria prevention program, with each of the various communities playing essential but unique roles. This malaria stakeholder meeting brought together numerous Service, specialty, COCOM and operational experts to strategize as to how the DoD's malaria program might be improved or optimized.

The entomology experts from the AFPMB shared recent developments, but despite these developments (and as demonstrated by our case study in Haiti), compliance with PPM is dependent upon command leadership and personal responsibility, and often is foiled by human nature. There exists the consistent need for greater training, leadership and risk communication—which the AFPMB has agreed to take for action. GEIS colleagues at the OCONUS labs aim to support the COCOMs and Education and Training commands through the development of malaria microscopy diagnostic training aids which will be incorporated into enlisted, officer and host nation microscopy training programs. Requirements will remain for just-in-time training and sustainment training to maintain microscopy proficiency. The malaria RDT, although a valuable resource, requires supporting clinical guidance and greater operational suitability so diagnostic support can be realized in austere conditions. AFIDS has agreed to assist with the development of a CPG to assist in the clinical assessment of fever/malaria. This CPG is merely one resource of many that should be jointly created and shared, reflecting a concerted Tri-Service effort. Participants concurred that Services should a) share existing malaria resources, b) collaborate to create new malaria resources, and c) coordinate to archive malaria resources in a common location. It was recognized that existing resources and training would benefit from greater marketing and visibility with the desire expressed for a "one-stop shop" where all resources could be available and readily accessed in support of knowledge management.

Perhaps the biggest accomplishment of this forum was the tackling of the malaria chemoprophylaxis issue. The need for a coherent malaria chemoprophylaxis policy was the predominant issue identified at the 2010 Inter-Agency Malaria Meeting via participant discourse and post-meeting surveys. This 2011 DoD Malaria Stakeholder meeting sought to address that need and drafted a proposal for deliberation. During the course of the forum, the main components of this policy were presented, opinions were shared, and accord was realized on several fronts. Draft verbiage was attained delineating Malarone® as a first line chemoprophylaxis medication in high-transmission areas. This revised language will be incorporated into the proposed policy, submitted to JPMPG for further staffing and ultimately routed to Health Affairs for approval of a DoD-level chemoprophylaxis policy.

This forum provided the opportunity to address several of these operationally relevant issues with critical stakeholders in attendance. Tremendous gains were realized with education and training, chemoprophylaxis policy, knowledge management, and understanding PPM compliance variables. Attendees were enthusiastic about the progress made at this meeting; strategies were outlined for each of the topics, with stakeholders agreeing to continue working independently to capitalize upon the momentum generated. Certainly there are growth opportunities still to be realized, but it is hoped that these conversations and ongoing efforts will have impact and will result in significant progress in further

meeting the needs of our warfighters and deployed medical personnel thereby diminishing the impact of malaria on U.S. Forces.

MEMORANDUM FOR ASSISTANT SECRETARY OF THE ARMY (M&RA)
ASSISTANT SECRETARY OF THE NAVY (M&RA)
ASSISTANT SECRETARY OF THE AIR FORCE (M&RA)
DIRECTOR OF THE JOINT STAFF

SUBJECT: Policy Memorandum on Medications for Prophylaxis of Malaria

References: (a) Memorandum, Assistant Secretary of Defense for Health Affairs, "Anti-Malarial Medications" October 17, 2002.
(b) Memorandum, Assistant Secretary of Defense for Health Affairs, "Policy Memorandum on the Use of Mefloquine (Lariam®) in Malaria Prophylaxis" September 04, 2009 (HA Policy 09-017).
(c) DODI 4150.07 "DOD Pest Management Program", May 29, 2008
(d) DODI 6490.03 "Deployment Health", August 11, 2006
(e) DoD Directive 6200.04 "Force Health Protection (FHP)", October 9, 2004.
(f) Army Regulation 40-562 / BUMEDINST 6230.15A / AFJI 48-110 / CG COMDTINST M6230.4F, "Medical Services Immunizations and Chemoprophylaxis", September 29, 2006.
(g) Centers for Disease Control and Prevention, Health Information for International Travel ("Yellow Book"), current edition.

1. Purpose

This document provides clarification of policy and best practices for the chemoprophylaxis (use of medication to prevent malaria) of service members serving in malaria endemic regions and augments reference (a). This document supersedes previous policies relating to the selection of medications for malaria chemoprophylaxis yet all annotated precautions should still be adhered to in accordance with reference (b).

2. Background

Malaria is caused by *Plasmodium* parasites and is transmitted by mosquitoes. Malaria prevention is achieved through personal protective measures, vector control, and chemoprophylaxis. Proper mosquito avoidance and the use of personal protection measures are discussed in references (c-d) and are not addressed in this policy. Chemoprophylaxis should be viewed as the last component of a comprehensive malaria prevention program, and serves as a final barrier to illness after bednets, insect repellants, permethrin-treated uniforms and personal clothing have been employed.

Chemoprophylaxis is administered as a force health protection measure under command authority as outlined in references (d-f) rather than as a part of routine medical care. Ensuring compliance with prophylaxis is a command responsibility.

3. Risk assessment
   a. For the purposes of this guidance, malaria risk is classified as high-transmission, low-transmission, or non-endemic as determined by the National Center for Medical Intelligence (NCMI; accessible at https://www.intelink.gov/ncmi/index.php). High-transmission refers to areas with an expected attack rate of 11% or more per month in the absence of countermeasures. Low transmission settings include all areas where NCMI risk assessments indicate a potential monthly attack rate of less than 0.1%, <1%, or 1-10% in the absence of countermeasures.

   b. Malaria transmission rates vary dramatically by geographic region. Some countries determined to have low transmission intensity might have focal areas with higher intensity. Units involved in operations in these areas might require countermeasures commensurate with higher transmission settings. Risk assessments should account for destination(s), accommodation(s), season(s), operational need(s), and itinerary.

   c. Pre-deployment evaluation should ascertain the most current malaria risk assessment for the intended itinerary, including NCMI malaria risk maps for each country, with the chemoprophylaxis regimen chosen accordingly. The Combatant Command Surgeon's office will be the adjudicating authority in determining high-risk areas within their area of responsibility.

4. Malaria chemoprophylaxis

Malaria chemoprophylaxis may be required for deployments where *Plasmodium falciparum*, *vivax*, *ovale*, and *malariae* strains may be encountered. *P. falciparum* is the most widespread, serious, and most commonly fatal type of malaria. FDA-approved medications available for malaria chemoprophylaxis are listed in Table1.

   a. High-transmission settings. Chemoprophylaxis is required for travel to high transmission areas. Atovaquone-proguanil (Malarone®) is recommended as the drug of choice for the prevention of malaria in these areas. For individuals unable to receive atovaquone-proguanil due to intolerance, contraindication, or nonavailability, doxycycline will be the preferred second-line therapy. Use of mefloquine prophylaxis is a third-line recommendation (due more to potential side effects than for efficacy/safety concerns) and should be restricted to individuals unable to receive either of the other regimens. Before using mefloquine as prophylaxis, care should be taken to exclude the presence of contraindications. Since chloroquine drug resistance is present throughout Africa

and Asia, chloroquine is inappropriate for prophylaxis in high-transmission areas on these continents.

b. Low-transmission settings. In general, operations in areas where potential attack rates are 0.1% per month or less do not require chemoprophylaxis. This is particularly true if there is little or no *P. falciparum* transmission or if the duration or nature of travel suggests a low likelihood of infection. For areas where monthly potential rates are assessed as greater than 0.1% but less than 11%, chemoprophylaxis is indicated when dusk until dawn exposures are anticipated. When chemoprophylaxis is to be used, the following guidance is provided.

    i. Chloroquine is the drug of choice for areas that are exclusively endemic with *P. vivax* malaria, or in those regions without chloroquine-resistant *P. falciparum* (e.g., Central America, Haiti, Saudi Arabia).

    ii. For areas with chloroquine-resistant *P. falciparum,* either doxycycline or atovaquone-proguanil are acceptable first-line prophylactic medications. Selection may be based on tolerance, unit uniformity, side-effect profile, individual preference, or desire for side benefits such as antibacterial activity of doxycycline. Individuals intolerant of the selected drug should receive the alternative first-line agent. Mefloquine should be reserved for individuals with intolerance or contraindications to both first-line medications. Before using mefloquine as prophylaxis, care should be taken to exclude the presence of contraindications.

c. Short-term travel. Regardless of destination, atovaquone-proguanil, due to its more favorable dosing regimen, should be considered for short-term travel (e.g. 2-3 weeks) or for those that travel frequently where the prolonged tail of doxycycline results in diminished compliance.

d. Although included as an acceptable alternative by the CDC, primaquine is not FDA approved for primary prophylaxis. Because this constitutes off-label use it can only be prescribed by a licensed medical provider on an individual basis rather than as a force health protection practice. Presumptive anti-relapse therapy (PART, or terminal prophylaxis) is an FDA-approved indication, but is not addressed in this policy.

e. Monitoring compliance with chemoprophylaxis is the responsibility of unit commanders. Directly observed therapy (DOT) is strongly recommended. This is especially important in austere conditions or in high-transmission areas.

5. Treatment Options:

Individuals with malaria should be treated with, and units should ensure availability of an FDA-approved drug from a different class than that used for prophylaxis. This selection should be drawn from the list of CDC treatment recommendations for that region, per reference (g).

6. Responsibilities

NCMI will review countries for malaria transmission risk annually. COCOMs will draft policy. Line commanders will ensure compliance with FHP measures.

Table 1. Chemoprophylaxis Regimens*

Drug	Dose	Dosing Instructions
Atovaquone-proguanil	250/100mg (1 tablet) daily	Begin 1-2 days prior to entry into malaria-endemic area. Continue daily dosing until 7 days after departure from malaria-endemic area.
Chloroquine	300mg (base) weekly	Begin 1–2 weeks prior to arrival to malaria-endemic areas. Take weekly on the same day of the week while in the malaria-endemic area and for 4 weeks after leaving such areas.
Doxycycline	100mg daily	Begin 1-2 days prior to travel to malaria-endemic areas. Take daily at the same time each day with food. Continue until 28 days after leaving malaria-endemic areas.
Mefloquine	228mg (base) weekly	Begin 1-2 weeks prior to arrival in malaria-endemic area. Take weekly during travel and continue for 4 weeks after departure from malaria-endemic area.

*Current product inserts should be referenced for contraindications.

Appendix 1: High-Transmission Countries *(as per July 2011)*:
(would not be included in the final draft, but here for your convenience)

- Angola
- Benin
- Botswana
- Burkina Faso
- Burma
- Burundi
- Cameroon
- Cape Verde (Sao Tiago only)
- Central African Republic
- Chad
- Comoros
- Cote d'Ivoire
- Democratic Republic of the Congo
- Republic of the Congo
- Djibouti
- Equatorial Guinea
- Eritrea
- Ethiopia
- Gabon
- the Gambia
- Ghana
- Guinea
- Guinea-Bissau
- Indonesia (portions)
- Kenya
- Laos
- Liberia
- Madagascar
- Malawi
- Mali
- Mauritania
- Mozambique
- Namibia (northeast only)
- Niger
- Nigeria
- Papua New Guinea
- Rwanda
- Sao Tome and Principe
- Senegal
- Sierra Leone
- Somalia
- South Sudan
- Sudan
- Swaziland (eastern portion)
- Tanzania
- Togo
- Uganda
- Zambia
- Zimbabwe

References: *(would not be included in the final draft, but here for your convenience)*

(a) Memorandum, Assistant Secretary of Defense for Health Affairs, "Anti-Malarial Medications" October 17, 2002.
http://www.pdhealth.mil/downloads/DASD_Letter_on_Antimalarials.pdf

(b) Memorandum, Assistant Secretary of Defense for Health Affairs, "Policy Memorandum on the Use of Mefloquine (LariamR) in Malaria Prophylaxis" September 04, 2009 (HA Policy 09-017).
http://www.health.mil/libraries/HA_Policies_and_Guidelines/09-017.pdf

(c) DODI 4150.07 "DOD Pest Management Program", May 29, 2008
http://www.dtic.mil/whs/directives/corres/pdf/415007p.pdf

(d) DODI 6490.03 "Deployment Health", August 11, 2006
http://www.dtic.mil/whs/directives/corres/pdf/649003p.pdf

(e) DoD Directive 6200.04 "Force Health Protection (FHP)", October 9, 2004.
http://www.dtic.mil/whs/directives/corres/pdf/620004p.pdf

(f) Army Regulation 40-562 / BUMEDINST 6230.15A / AFJI 48-110 / CG COMDTINST M6230.4F, "Medical Services Immunizations and Chemoprophylaxis", September 29, 2006. http://www.vaccines.mil/documents/969r40_562.pdf

(g) Centers for Disease Control and Prevention, Health Information for International Travel ("Yellow Book"), current edition.
http://wwwnc.cdc.gov/travel/yellowbook/2012/table-of-contents.htm

Comparison of Malarone® versus doxycycline for chemoprophylaxis of malaria in US military populations

BLUF: Atovaquone-proguanil (Malarone®) should be the drug of choice for malaria chemoprophylaxis for military deployments of short duration (up to 3 weeks) or to areas with high malaria transmission (e.g., sub-Saharan Africa) based on its greater efficacy, effectiveness, tolerability, safety profile and its lower risk of breakthrough. Doxycycline may have an advantage in certain occupational groups or specifically in those operational environments with a high risk of leptospirosis and rickettsial infections.

Rationale for selection of atovaquone-proguanil (ATQ-Pro) as the military malaria chemoprophylaxis drug of choice:

- ATQ-Pro is better tolerated than doxycycline in randomized, double-blind, placebo-controlled trials.
- ATQ-Pro has an excellent safety record with very few serious adverse events reported in 10 years of extensive use. There are few, if any, known drug interactions of importance with ATQ-Pro.
- The rationale is particularly strong for using ATQ-Pro for travel of short duration and to areas of high malaria risk because of its advantage in patient compliance with post-exposure prophylaxis and the concern with the risk of breakthrough with doxycycline—particularly in austere conditions. For short-term deployments to any location (up to 3 weeks) and for all deployments to sub-Saharan Africa (very high risk), ATQ-Pro should be the drug of choice for the prevention of malaria.
- There are no concerns with weight dependence for dosing with ATQ-Pro. Doxycycline at 100 mg daily dose has never been tested in non-immune adults greater than 70 kg. 100 mg daily dose of doxycycline may fail in large individuals, especially those greater than 100 kg. In fact, doxycycline efficacy has been shown to be dose dependent in Thailand (100 mg better than 50 mg) so a weight-dependent dose for doxy efficacy is likely.
- Post-exposure prophylaxis tail is only 7 days with ATQ-Pro whereas doxycycline requires 28 days of post-exposure prophylaxis. Directly observed treatment post-deployment in CONUS is very difficult to achieve. Effectiveness of post-exposure ATQ-Pro at 7 days will be much greater than 28 days of doxycycline in this non-observed (and presumably less compliant) setting. In fact, just one 250/100 mg tab of ATQ-Pro pre- or post-exposure has been demonstrated to prevent malaria.
- Currently, atovaquone-proguanil (Malarone®) is only available as a branded drug from GSK. A generic formulation is expected to become available sometime in 2012. Generic pricing remains to be determined.

Supporting documentation and cross-comparison between Malarone® and doxycycline is provided in the table below. Green shading indicates a more favorable advantage; gray boxes designate no significant advantage to either medication.

Criterion	Malarone[a]	Doxycycline[b]	Comments
Cost			
Per pill	$3.83	$0.05	
For a 3 week trip	$107.24 (21+7 = 28 pills)	$2.45 (21+28 = 49 pills)	
Efficacy: controlled clinical trials with directly observed therapy (DOT)			
Prevention of *P. falciparum* malaria	> 97-100%	> 95%	Refs 1, 2.
Prevention of primary *P. vivax* malaria	84% (CI 44-95%)	76-100%	Limited data on prevention of *P. vivax* for both drugs (Refs 1, 2).
Prevention of *P. vivax* or *ovale* relapse when used as primary prophylaxis	No	No	Neither drug has any anti-hypnozoite activity.
Dose appropriate regardless of body weight	Yes	Concerns	Doxycycline at 100 mg daily dose has never been tested in non-immune adults > 70 kg. (Table 1, Ref 1). 100 mg daily dose may

			fail in large individuals, especially >100 kg. Doxycycline efficacy shown to be dose dependent in Thailand (100 mg better than 50 mg) so a weight dependent dose for efficacy is suggested (Ref 3). See References 1, 3, 4, 5.
Mechanism of Action			
Affects blood stage parasites	Yes	Yes	Prophylactic doses of both drugs are insufficient for treatment of blood-stage malaria.
Affects liver stage parasites	Yes	Partially	Explains why Malarone® can be given for just 7 days post-exposure. Without post-exposure dosing, doxycycline efficacy for *P. falciparum* is 67% (8/12 cases; Ref 6).
Effectiveness: Real world use (usually without DOT)			
Pre-travel regimen	1-2 days prior	1-2 days prior	Refs 1, 2.
During travel regimen	Daily	Daily	Refs 1, 2.
Post-travel regimen	7 days after	28 days after	Good data with Malarone® demonstrating that a single pill taken when departing a malarious area is effective (Refs 7, 8). Good data with doxy to show 28 days needed post-exposure. Surge in cases noted 3 weeks after discontinuing field trials of doxy prophylaxis (Refs 3, 5).
Risk of breakthrough with missed or delayed doses	Rare	Occurs	Falciparum malaria prophylaxis breakthrough with Malarone® has rarely been reported (not confirmed). Falciparum malaria prophylaxis breakthrough with doxycycline is common (nonadherence frequently implicated).
Ease of DOT in US military populations *(Weekly assumed better than daily)*	Daily	Daily	Command discipline easier to enforce with weekly dosing. Should strive for once weekly DOT with pill checks and educational reinforcement.
Public perception or adverse publicity with use of medications	No	No	None as compared to mefloquine related issues. Bad publicity may affect compliance.
Risk of adverse publicity with policy change from doxy to Malarone® as drug of choice	No	No	None anticipated from the general public, but acknowledge DoD stakeholders may question the extra expense of Malarone®.

Appendix B: White Paper: Comparison of Doxycycline vs. Malarone®

Resistance			
Geographic areas with known resistance	No	No	Either drug can be used in any geographic location without worry of parasite resistance.
Safety			
Contraindications (per label)	Known hypersensitivity; severe renal impairment (creatinine clearance <30 mL/min).	Known hypersensitivity.	Rare for both drugs.
Serious adverse events (SAEs) as defined in the current product insert	None	None	SAEs as defined in 21CFR312.32 and listed in product insert.
Uncommon / rare serious side effects (post-licensure)	Erythema multiforme (EM), Stevens Johnson syndrome (SJS).	Esophageal perforation, mediastinitis, rarely death.	Malarone®-related EM and SJS cases have been mild with no fatalities; did not require steroids or hospitalizations (Ref 2). Deaths due to mediastinitis secondary to esophageal perforation with doxycycline hyclate have been recorded. France removed doxycycline hyclate from the market for safety concerns and doxy monohydrate was made available with a better safety record (Ref 1).
1st trimester of pregnancy	Limited data, FDA category C (CDC does not recommend but may be used after assessing patient's risk / benefit.	Limited data, FDA category D (CDC does not recommend).	Issue for US military is 1st trimester pregnancy while taking prophylaxis. Atovaquone and proguanil both have excellent safety records in 1st trimester pregnancy as individual medications.
Drug-Drug interactions			
Common interactions	Diminished peak serum levels of atovaquone with tetracyclines.	All divalent cations (Al^{2+}, Ca^{2+}, Mg^{2+}) containing drugs (antacids) interfere with GI tract absorption of doxy and may lead to breakthrough. Milk and dairy products should not be ingested concurrently.	Refs 1, 2.
Tolerability			
% discontinuing medication in controlled clinical trials	1%	5%, higher if ingested without food.	Refs 1, 2.

Gastrointestinal side effects	Occasional	Mild to moderate nausea (4–33%), abdominal pain (12–33%). Nausea noted to be more common when doxy is ingested without food. Vomiting (4–8%) and diarrhea (6–7.5%) are less commonly reported.	Refs 1, 2.
Oral ulcerations	1-2% oral ulcers due to proguanil	Not reported	Refs 1, 2.
Photosensitivity	Not reported	7-21%	Refs 1, 2.
C. difficile colitis	Not reported	Reported	Refs 1, 2.
Gender-specific side effects	None	5% vaginal candidiasis	Refs 1, 2.
Operationally Important Criteria			
Flight restrictions	Ground Trial	None	Service policy may require a single 48-hour ground trial with initial dose of Malarone®.
Dive restrictions	None	None	Per BUMED.
Barriers to use for frequent short travel (e.g., pilots, SOC)	Minimal	Significant	Doxycycline 28-day post-exposure dosing is problematic.
Prevents leptospirosis and rickettsial infections	No	Yes	Refs 9, 10.

a. Malarone® currently is the only available form of atovaquone-proguanil.
b. Doxycycline refers to generic doxycycline hyclate available from numerous suppliers. Although not presented, doxycycline monohydrate would have a similar profile but with diminished GI side effects, an improved tolerance and safety record, and an increased cost estimate ($1/pill).

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3) Pang L et al. Prophylactic treatment of vivax and falciparum malaria with low-dose doxycycline. J Infect Dis. 1988 Nov;158(5):1124-7.

4) Pang L. Doxycycline prophylaxis for malaria. Lancet. 1987 Oct 24;2(8565):970.

5) Pang LW et al. Doxycycline prophylaxis for falciparum malaria. Lancet. 1987 May 23;1(8543):1161-4.

6) Shmuklarsky et al. Failure of doxycycline as a causal prophylactic agent against Plasmodium falciparum malaria in healthy nonimmune volunteers. Ann Intern Med. 1994 Feb15;120(4):294-9.

7) Shapiro TA et al. Prophylactic activity of atovaquone against *Plasmodium falciparum* in humans. *Am J Trop Med Hyg.* 1999 May;60(5):831-6.

8) Deye et al. Prolonged Protection Provided by a single dose of Atovaquone/Proguanil for the Chemoprophylaxis of Plasmodium falciparum Malaria in a Human Challenge Model (Manuscript in press CID)

9) Takafuji ET et al. An efficacy trial of doxycycline chemoprophylaxis against leptospirosis. N Engl J Med. 1984 Feb 23;310(8):497-500.

10) Twartz JC et. al. MG. Doxycycline prophylaxis for human scrub typhus. J Infect Dis. 1982 Dec;146(6):811-8.

Appendix C: Consensus Verbiage for High-Risk Guidance for Draft Chemoprophylaxis Policy

Proposed HA Memo--

SUBJECT: Policy Memorandum on Medications for Prophylaxis of Malaria

"Consensus" paragraph re-write for paragraph 4a.

4. Malaria chemoprophylaxis

   a. High-transmission settings. Chemoprophylaxis is required for travel to high transmission areas. Atovaquone-proguanil (Malarone®) is recommended as the drug of choice for the prevention of malaria in these areas. For individuals unable to receive atovaquone-proguanil due to intolerance or contraindication, doxycycline will be the preferred second-line therapy. Use of mefloquine prophylaxis is a third-line recommendation (due more to potential side effects than for efficacy/safety concerns) and should be restricted to individuals unable to receive either of the other regimens. If mefloquine is chosen as prophylaxis, practice as defined in the following paragraph will be followed… *[Insert appropriate language from HA Policy 09-017].* Since chloroquine drug resistance is present throughout Africa and Asia, chloroquine is inappropriate for prophylaxis in high-transmission areas on these continents.

Appendix D: Inventory of DoD and Services' Tropical Medicine Training

Tropical Medicine Training Opportunities

Deployment and International Health Short Course
http://wrair-www.army.mil/OtherServices_TropicalMedicine.aspx

Description: *Intensive and targeted short course in deployment and international infectious disease threats concentrated on individuals operating with limited or sporadic tropical and infectious disease consultative support. The course was created in response to the need of a short course on tropical medicine by AFRICOM and the special forces community. This curriculum was designed to educate medical personnel by providing them with the skills and training they need to tackle tropical infectious diseases in austere environments while deployed or working in overseas labs. This hands-on course was designed to familiarize students with tropical diseases they may encounter overseas. The morning didactic sessions will consist of world-class experts presenting on tropical diseases that military personnel may encounter while deployed or while working at an overseas laboratory. The afternoons will consist of hands-on laboratory sessions with a focus on deployment-relevant diagnostics.*

Audience: United States military service physicians, physician assistants, nurse practitioners, ESOs, 18D medics, 91S preventive medicine technicians, or other medical personnel. This course is open to civilians, other government agencies and foreign nationalists that are involved in the medical health field (subject to approval).

Location: WRAIR, Silver Spring, MD

Length: 2 weeks

Global Medicine Course (GM)
https://www.us.army.mil/suite/page/649028

Description: *Part of the U.S. Military Tropical Medicine program (MTM) and led by the USAF School of Aerospace Medicine, the Global Medicine (GM) course is a two week educational activity designed to prepare deploying medical personnel for a wide range of operational requirements through a combination of lectures and laboratory exercises. Its goal is to provide relevant global health and operational medicine content to deploying medical personnel. In addition to providing instruction on traditional disease topics such as hepatitis and diarrhea, malaria, sexually transmitted infection, and intestinal parasitic infections, the course emphasizes successful design and implementation of a plan that minimizes the health risk of the endemic natural biologic hazards to a deploying or deployed force.*

Audience: Allied Health personnel including IDC and physicians anticipating assignment to operational settings.

Location: Wright Patterson AFB, Ohio

Length: 2 weeks

Military Tropical Medicine (MTM)—Didactics
https://www.us.army.mil/suite/page/649028

Description: *Part of the U.S. Military Tropical Medicine program (MTM) and led by the Navy Medicine Professional Development Center, this four-week curriculum covers a broad range of topics in tropical diseases and other health issues working in the developing world, with corresponding laboratory sessions, including helminths, malaria and other protozoa. There is a comprehensive lab practical and written exam at the end of the course, as well as weekly lab quizzes. Faculty come from leading civilian and military programs and includes international experts.*

Audience: Physicians from the Army, Navy and Air Force may apply. Priority is given to those in operational billets and for whom the course is an integral part of established training.

Location: USUHS, Bethesda, MD

Length: 4 weeks

Military Tropical Medicine (MTM)—Field
https://www.us.army.mil/suite/page/649028
Description: *Part of the U.S. Military Tropical Medicine program (MTM) and led by the Navy Medicine Professional Development Center, this course is an advanced in-field, mentored deployment for training during which students practice*

interactions with US agencies, non-governmental organizations and host governments working towards improved health in the developing world.

Audience: Physicians from the Army, Navy and Air Force who are applying for MTM-Didactics in the same fiscal year or who have successfully completed MTM-Didactics within the previous four years may apply.

Location: Mission sites vary, but have recently included Paraguay, Ghana, Guyana, Honduras, Kenya and Peru.

Length: 2 weeks

Military Tropical Medicine (MTM)—Just in Time Training: Distributed Operations
https://www.us.army.mil/suite/page/649028

Description: *Commands deploying or deployed to the developing world may request this MTM traveling export, part of the U.S. Military Tropical Medicine program (MTM) and led by the Navy Medicine Professional Development Center. Senior MTM program faculty members tailor the curriculum to the needs of the operational unit and teach it in the context of impending or on-going operations. The curriculum covers mission planning, malaria, waterborne exposures, rickettsioses, helminthes, arboviruses, clinical laboratory and microscopic identification practicums. The modality is interactive and responsive, addressing elements of implementing force health protection and medical stability operation tasks in their resource limited setting.*

Audience: Deployed or deploying medical personnel including the range of Allied Health and IDC.

Location: Teaching sites vary.

Length: Varies by need of requesting command, 1-7 days

Training in Tropical Medicine and Traveler's Health
http://www.usuhs.mil/pmb/divisions/tph/tphtraining.html

Description: *This comprehensive course is comprised of a lecture, seminar, laboratory, and case-based curriculum and is designed to provide expertise in travel and clinical tropical medicine. The course covers laboratory and radiologic diagnosis, treatment, prevention and control of disease, and local medical customs and healthcare structure. This USUHS course offering is certified as an American Society of Tropical Medicine and Hygiene (ASTMH) Diploma Course and it fulfills the eligibility requirements for physicians to take the ASTMH Certificate of Knowledge Examination.*

Audience: DoD/U.S. Government employees and civilian medical providers who want to improve their practice of tropical and travel medicine.

Location: USUHS, Bethesda, MD

Length: 3 months

USU/AFHSC Infectious Disease Training Program
http://www.usuhs.mil/pmb/divisions/tph/tphtraining.html

Description: *This overseas opportunity improves the preparedness of Uniformed Services medical personnel to face tropical infectious disease challenges and to perform research or disease surveillance in an international setting. Participants spend 4 weeks on a sponsored rotation working closely with a clinical or research mentor.*

Audience: Uniformed Services officers with a strong interest in public health, research, or clinical career paths to include medical students, residents, physicians, fellows, and graduate students.

Location: DoD overseas medical research laboratory or other location

Length: 4 weeks

For additional information on tropical medicine and humanitarian assistance training opportunities please refer to:
Coldren RL, Brett-Major DM, Hickey PW, Garges E, Weina PJ, Corrigan P, Quinnan G. Tropical Medicine Training in the Department of Defense. *Military Medicine*. 2012; 177(4): 361-363.

DoD Malaria Microscopy Training for Medical Enlisted Training (MET) Instructors

PROBLEM: The lack of prompt malaria diagnosis in the deployed setting results in excessive morbidity, mortality and med-evac costs and thereby adversely impacts readiness and mission completion.

BLUF: Improved malaria microscopy proficiency of deployed medical personnel via training at MET will improve the clinical care of deployed Service members.

BACKGROUND:

- Malaria remains the #1 DoD infectious disease threat to the deployed Service member.
- Despite microscopy being the gold standard, deployed forces rely heavily on the current FDA approved rapid diagnostic test (RDT) or local (host nation) microscopists to diagnose malaria infections. For non-immune Service members the RDT can have low sensitivity in the initial stages of falciparum malaria, resulting in false negative results. Likewise, the local national microscopists have varying levels of training and proficiency, potentially resulting in high false negative rate especially in the early stages of malaria infection.
- Malaria diagnosis by microscopy is an acquired skill, highly technical and easily perishable.
- Microscopy expertise resides at each of the five OCONUS research labs that are an integral part of the GEIS partner network. These experts regularly review thousands of malaria smears by microscopy each year and are a tremendous DoD asset.
- Microscopists' expertise could be leveraged by training deploying healthcare personnel so that they might more adeptly diagnose and treat malaria cases in the austere deployed environment.

DISCUSSION:

- Proposal: Utilize DoD OCONUS expert microscopists to provide specialized technical training in malaria diagnostics to laboratory instructors to improve the proficiency of medics and corpsmen graduating from Medical Enlisted Training. Train-the-trainer construct will provide the most impact, sustainment, and best dollar value.
- Initial training will consist of a 5-day Basic Malaria Microscopy Course for MET instructors that will provide background information about the malaria threat, techniques for proper blood smear preparation, malaria parasite identification and speciation. The course will be offered to new MET instructors at 6 month intervals.
- Sustainment training consists of a 2-day Refresher Course for previously trained MET instructors and will be provided at 6 month intervals.
- Scope: Proficiency will be documented by pre- and post-test evaluations. Training will be funded for a 2-year trial by the Armed Forces Health Surveillance Center (AFHSC). An analysis of the training will be conducted at the end of the second training event with a report generated and issued to all stakeholders. A favorable review and analysis will result in a formal proposal to the training command for permanent incorporation of microscopy training into the curriculum.
- Anticipated Costs: 3-4 instructors will require travel expenses and an average of 7 days of per diem per year. Consumables will be limited to a minimal amount of laboratory supplies and reagents to make peripheral blood smears.

RECOMMENDATION:

- Pursue a 2-year trial of an AFHSC-funded train-the-trainer microscopy skills course for MET instructors to amplify the expertise of DoD microscopists thereby improving the proficiency of Phase I students at MET.

Appendix F: Inventory of DoD and Services' Malaria Resources

Malaria Education and Training Resources

AIR FORCE RESOURCES

- DIAGNOSING MEDICAL PARASITES: A Public Health Officers Guide to Assisting Laboratory and Medical Officers
  http://www.afpmb.org/sites/default/files/whatsnew/2009/Diagnosing_Medical_Parasites.pdf

ARMY RESOURCES

Malaria Guide coming soon!

Fact Sheets:

- USAPHC Just the Facts – Falciparum Malaria, Apr 10
  http://phc.amedd.army.mil/PHC%20Resource%20Library/MalariaFalciparumApr2010.pdf
- USAPHC Just the Facts - Malaria, Jan 07
  http://phc.amedd.army.mil/PHC%20Resource%20Library/18-040-0107_Malaria[1].pdf
- USAPHC Just the Facts - Vivax Malaria, Jan 10
  http://phc.amedd.army.mil/PHC%20Resource%20Library/MalariavivaxJan2010.pdf
- USAPHC Just the Facts - Doxycycline – Deployment Medication Information Sheet, Jun 06
  http://phc.amedd.army.mil/PHC%20Resource%20Library/Doxycycline_DMIS_FS_final_Jun06.pdf

Deployment Health Resources:

- USACHPPM Tech Guide 248: Guide for Deployed Preventive Medicine Personnel on Health Risk Management
  http://usaphcapps.amedd.army.mil/HIOShoppingCart/Uploads/DownloadableProds/121_FG_TG248.pdf

Entomology Resources:

- Entomology posters and cards in the shopping cart:
  https://usaphcapps.amedd.army.mil/HIOShoppingCart/searchResults.aspx?c=4&s=26&f=0&l=0&t
- Vector-borne prevention information (to include Malaria) is routinely included in Deployment Health Products- to include Medical threat briefs (MTBs) and Deployment Health Guides and Cards
  - MTBs also has some vector-borne and maps if applicable
    https://www.us.army.mil/suite/doc/28777897]\ (slides 28-32)
- Personal Protective Measures educational material
  http://usaphcapps.amedd.army.mil/HIOShoppingCart/searchResults.aspx?c=0&s=0&f=0&l=0&t=malaria
  To include posters, flyers, tip cards, etc.
- Also, Entomology & Pest Management webpage
  http://phc.amedd.army.mil/topics/envirohealth/epm/Pages/default.aspx
  Info on DoD Insect Repellant System, Flame-Resistant Army Combat Uniform- Permethrin, etc.

NAVY RESOURCES:

NMCPHC Malaria Webpage:
http://www.nmcphc.med.navy.mil/Diseases_Conditions/malaria.aspx

Malaria Resources:

- 2011 Pocket Guide to Malaria Prevention and Control (Technical Manual NMCPHC-TIM 6250.1)
  http://www.nmcphc.med.navy.mil/downloads/prevmed/malaria/NMCPHC_Malaria_PocketGuide_2011.pdf
- Malaria Prevention & Control Presentation
  http://www.nmcphc.med.navy.mil/downloads/prevmed/malaria/Malaria_NEHC-IDC_2005_%20post_revision.ppt

Appendix F: Inventory of DoD and Services' Malaria Resources

Training:

- On-line Malaria training course [#NMCPHC-MPC-1.1]
  The Malaria Prevention and Control course provides a detailed presentation of malaria, its life cycle and its control by means of personal protective measures and chemoprophylaxis and is required for all Navy personnel deploying to AFRICOM.
- Laboratory Identification of Malaria [#B-322-2210]
  1-day microscopy course taught by NEPMUs.

Pest Management Resources:

- NMCPHC Pest Management Webpage
  http://www.nmcphc.med.navy.mil/Preventive_Medicine/pestmanagement.aspx
- NAVMED P-5010-8: Navy Entomology and Pest Control Technology
  http://www.nmcphc.med.navy.mil/downloads/prevmed/west_nile/P-5010-8.pdf

DoD RESOURCES:

Deployment Health Clinical Center: Malaria Webpage
http://www.pdhealth.mil/malaria.asp

Fact Sheet:

- DoD Fact Sheet: Mefloquine (Lariam®) Information for Clinicians
  http://www.nmcphc.med.navy.mil/downloads/prevmed/malaria/Mefloquine.doc

DoD Entomology Resources:

- Armed Forces Pest Management Board Technical Guide No. 36 : Personal Protective Measures Against Insects and Other Arthropods of Military Significance
  http://www.afpmb.org/sites/default/files/pubs/techguides/tg36.pdf
  There is some historical information on malaria as well as a great overview of the personal protective measures, repellents and material available in the National Stock Number (NSN) system for combating mosquitoes published by the AFPMB in the form of a Technical Guide.
- Armed Forces Pest Management Board (AFPMB) Standard Pesticides List Available to DoD Components and Agencies http://www.afpmb.org/sites/default/files/pubs/standardlists/DOD_PESTICIDES_LIST.pdf
  The most up-to-date list of arthropod repellents available in the NSN system.
- AFPMB Interactive Programs for Teaching Adult Mosquito Morphology, Larval Mosquito Morphology (CD-ROMS) http://www.afpmb.org/teaching-cds
- DoD Pest Management Materiel List (Other Than Pesticides)
  http://www.afpmb.org/sites/default/files/pubs/standardlists/DOD_PEST_MANAGEMENT_MATERIAL_LIST.pdf
  Equipment for trapping mosquitoes, including light traps, are available in the NSN system and can be found listed on the AFPMB website
- Malaria Sporozoite Antigen Panel Assay (NSN information and package insert)
  http://www.afpmb.org/sites/default/files/pubs/standardlists/equipment/pdfs/6550-01-551-5327.pdf
  http://www.afpmb.org/sites/default/files/pubs/standardlists/equipment/pdfs/6550-01-551-5327_instructions.pdf
  There is the dipstick test available for use in the field for quickly testing Anopheles mosquitoes caught in light traps for infection with Plasmodium falciparum or Plasmodium vivax malaria parasites available in the NSN system

DISCLAIMER: May not represent a comprehensive list of available resources, but reflects what was provided by Service representatives. Service, COCOM, and DoD policies intentionally omitted but could/should be added to the inventory of resources available to encourage "one-stop" availability.

Appendix G: Acronyms

AFHSC	Armed Forces Health Surveillance Center
AFIDS	Armed Forces Infectious Diseases Society
AFN	Armed Forces Network
AFPMB	Armed Forces Pest Management Board
AFRIMS	Armed Forces Research Institute for Medical Sciences
AMISOM	African Union Mission in Somalia
AOR	area of responsibility
BUMED	Navy Bureau of Medicine and Surgery
CAC	Common Access Card
CDC	Centers for Disease Control and Prevention
COCOM	Combatant Commands
CPG	clinical practice guideline
DEET	Diethyl-*m*-toluamide
DHCC	Deployment Health Clinical Center
DoD	Department of Defense
DOT	directly observed therapy
FDA	Food and Drug Administration
FHP	force health protection
GEIS	Global Emerging Infections Surveillance and Response System
GMO	general medical officer
IC_{50}	Inhibition Concentration (reduced 50%)
IDSA	Infectious Diseases Society of America
IND	investigational new drug
ISTM	International Society of Travel Medicine
IV	intravenous
JBAIDS	Joint Biological Agent Identification and Detection System
MDC	Malaria Diagnostics Center
MEF	Marine Expeditionary Force
METC	Medical Education and Training Campus
MSMR	Medical Surveillance Monthly Report
MSSC	Malaria Surveillance Steering Committee
MTF	military treatment facility
NAMRU-2	Navy Medical Research Unit, Cambodia
NAMRU-6	Navy Medical Research Unit, Lima, Peru
NATO	North Atlantic Treaty Organization
NCMI	National Center for Medical Intelligence
NDA	new drug application
NIH	National Institutes of Health
NMCPHC	Navy & Marine Corps Public Health Command

Appendix G: Acronyms

OCONUS	outside the continental U.S.
OSD/HA (FHP&R)	Office of the Secretary of Defense/Health Affairs (Force Health Protection & Readiness)
PCR	polymerase chain reaction
PMSMO	Pharmaceutical Systems Project Management Office
PPE	personal protective equipment
PPM	personal protective measures
QTc	QT interval (corrected)
R&D	research and development
RDT	rapid diagnostic test
USAFRICOM	U.S. African Command
USAMMDA	U.S. Army Medical Materiel Development Activity
USAMRMC	U.S. Army Medical Research and Materiel Command
USAMRU-K	U.S. Army Medical Research Unit – Kenya
USAPHC	U.S. Army Public Health Command
USCENTCOM	U.S. Central Command
USPACOM	U.S. Pacific Command
USSOUTHCOM	U.S. Southern Command
USSOCOM	U.S. Special Operations Command
USUHS	Uniformed Services University of Health Sciences
WHO	World Health Organization
WRAIR	Walter Reed Army Institute for Research